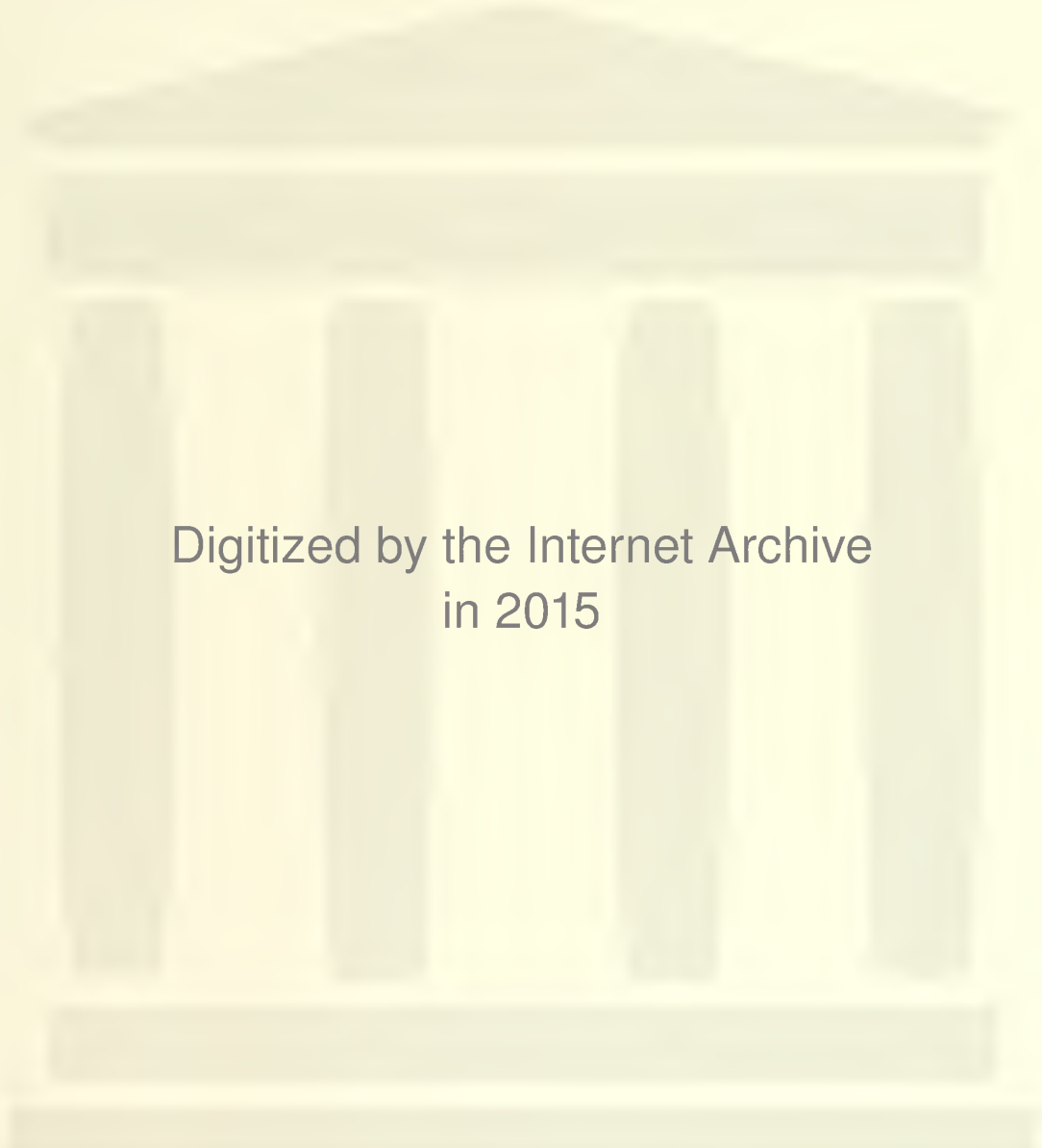
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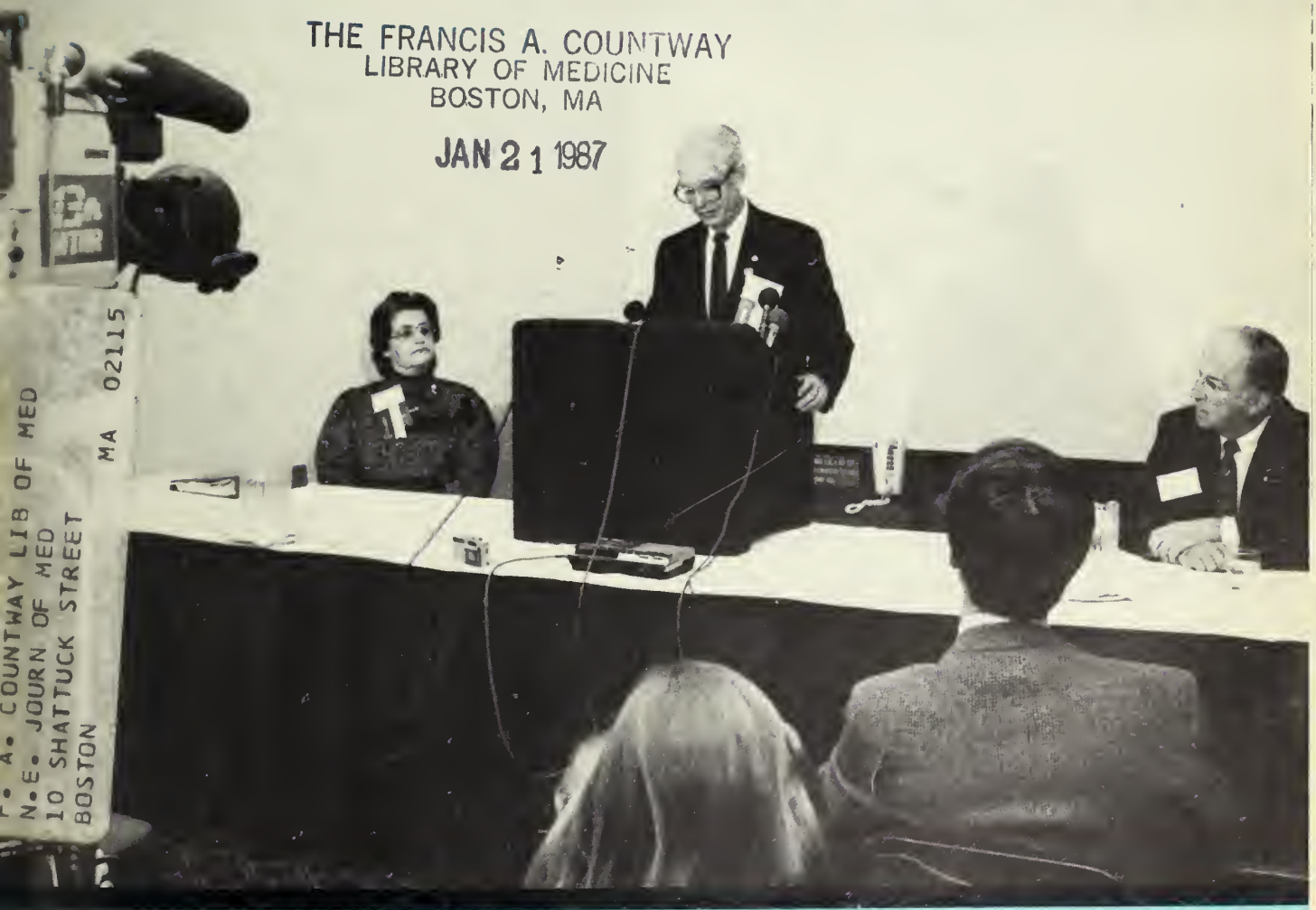
NEW FRONTIERS IN MEDICAL CARE

JANUARY 1987 VOL. 80 NO. 1

INDIANA MEDICINE

The Journal of the Indiana State Medical Association

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In This Issue.....

COVERAGE OF THE 1986 ISMA CONVENTION

FOR MEDICAL PROFESSIONAL LIABILITY COVERAGE, THE ISMA STRONGLY RECOMMENDS PHYSICIANS INSURANCE COMPANY OF INDIANA. Several companies are anxious to provide most Indiana physicians with medical professional liability insurance coverage. *Only one* has received the formal endorsement, support, and sponsorship of the Indiana State Medical Association. That company is PICI, Physicians Insurance Company of Indiana.

Why PICI?

Because PICI is committed to providing Indiana physicians with the best possible coverage at the lowest possible rates throughout their medical careers. Indiana physicians dominate the company's board of directors and serve on budget, claims and underwriting committees. PICI is a publicly held stock company, and provides annual as well as periodic interim financial reports.

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Vol. 80, No. 1
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Devoted to the interests of the medical profession and public health in Indiana since 1908.

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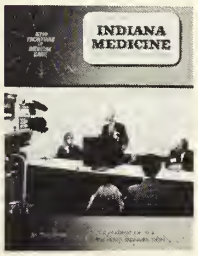
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ABOUT THE COVER

Thirty-three TV, radio and newspaper reporters were attracted to the 1986 ISMA convention. Here, the media cover remarks during a press conference featuring Dr. Paul Siebenmorgen (standing), Dr. Shirley Thompson Khalouf, and Dr. John J. Coury, AMA president. Our coverage of the convention begins on page 50.—PHOTO BY ED LACEY JR.

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MEDICAL MUSEUM NOTES



CHARLES A. BONSETT, M.D., Indianapolis

CALVIN FLETCHER, writing in his diary for July 22, 1861, describes his reaction to the first major conflict of the Civil War, known in the North as the First Battle of Bull Run (named for the stream that flows through the area) and in the South as First Manassas (named for the town of Manassas Junction). The battle had been fought the previous day.

"This morn dispatches (were) favorable as to our army . . . But at 2 p.m. very sad intelligence that the army at Bull Run had taken a fright and run and that the army were advancing on Washington. All sad and shocked me much. So much so that I could scarcely stand up. No private calamity I ever experienced ever so overwhelmed me. I believe I did nothing all of p.m. Sent for Bishop Ames. He and I both felt it the duty to fall before the Lord, that great national sins had to be attoned for."

Another person who had occasion to take pen in hand on July 22, 1861, was Dr. John S. Bobbs, who had been appointed as Indiana's Surgeon-General. He was in Washington, D.C. at that time at the request of General Thomas A. Morris, commander of the First Brigade, and was reporting back to his chief, Governor Oliver P. Morton.

"Washington City, July 22, 1861

"His Excellency, Gov. O.P. Morton.

"Dear Sir:

"I arrived in Washington this morning in discharge of a little commission from Gen. Morris. The excitement here consequent upon the recent engagement is intense and pervading, so great, indeed, that particulars in reference to it are difficult to collect.

"It is believed here that Gen. Patterson failed in his duty to prevent a juncture of Gen. Johnston's force with that of Gen. Beauregard by which the whole force of both columns of the enemy were engaged with the single one on our side. The enemy also maintained themselves under cover during the whole contest, which lasted all day, never emerging into open view and depending upon masked batteries as their most effective weapons.

"On the other hand, our troops generally had made laborious marches, by which they were greatly exhausted before they came into action. They universally attest that the only thing they had to direct their fire was the smoke of the enemy's guns. The Fire Zouaves (Col. Ellsworth) and the 79th Pennsylvania and the 69th New York seem, so far as I can gather, to have been the chief sufferers. The first are believed to have had from two-thirds to three-fourths of their number killed or wounded.

. . . This Is Undoubtedly the Most Terrible Engagement Ever Fought upon This Continent . . .'—J.S. Bobbs, M.D.

"The remnant in the city is hardly a full company of the whole regiment, but others may yet turn up. Several other regiments lost nearly all their field and company officers, and their comrades are so decimated and scattered, their true condition is not known yet. Col. Cameron of the 79th, my brother-in-law, was killed and his body not yet recovered, but hopes are entertained that it will be, as extraordinary efforts were made to bring it off the field by the remnants of his regiment.

"Col. Sherman lost his battery, as did the Rhode Island brigade, except one gun. The former, however, afterwards recovered his after a successful charge and brought it off. A portion of the troops maintained the fire of the enemy with extraordinary courage and coolness, but we believe this was not universal among them. Still, the result is too recent and the facts too imperfectly understood to speak with certainty on this point.

"The terrible courage of the Fire Zouaves in a charge on masked batteries! They were literally cut to pieces. Altogether this is undoubtedly the most terrible engagement ever fought upon this continent, the loss in killed and wounded being estimated at 2,500 to 3,000; it was very disastrous to our forces, as many officers and men have fallen. Our forces remain in possession of their ground, having been reinforced by Gen. Butler at the close of the engagement. No fears are entertained of this city, so far as I know. We are now most likely to have war in earnest.

"Respectfully,

"(signed) J.S. Bobbs"

It is not clear what Dr. Bobbs' "little commission" from General Morris was. Perhaps it is clarified by an article that Calvin Fletcher clipped from the *Cincinnati Gazette* and pasted in his diary:

"Our surgeons had busy work for a time . . . Dr. (William B.) Fletcher (a son of Calvin) of Indianapolis, who was acting as an aide to General Morris . . . rendered efficient services on the field, and dressed wounds with an utter recklessness of the occasional bullets whistling nearby. Surgeon-General (John S.) Bobbs (was) . . . particularly useful in caring for the wounded of the rebel forces. . . ."

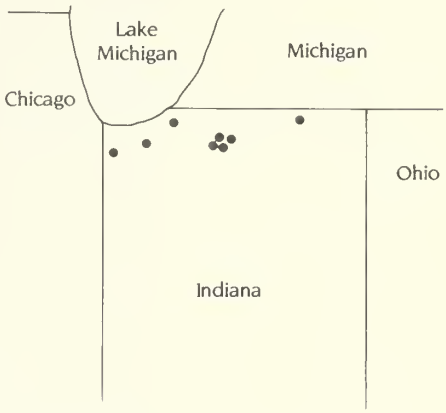
It is of interest that with the passing of eight years (1869) John Bobbs and William B. Fletcher would again be working together, in founding the Indiana Medical College, the oldest and largest of the proprietary schools whose union would give origin to Indiana University School of Medicine.

Dr. Alembert W. Brayton (1848-1926), shown in the illustration, is the source of this letter to Bobbs. Dr. Brayton served as physician to Mrs. Oliver P. Morton for nearly 25 years. She gave the letter to Dr. Brayton, who in turn gave it to Dr. Henry Jameson. Whether the letter survives to the present is unknown. Dr. Brayton published it in the *Indianapolis Medical Journal* (Vol. XX, pp 175-176, 1917). It is doubtful that even this publication can be found today outside of the medical school library. Dr. Brayton was the first professor of dermatology at I.U.S.M. He was elected president of the ISMA in 1901.

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What you should know about Meridian Healthcare services and facilities.

Meridian Healthcare operates eight major facilities in northern Indiana—five of which are clustered in and near St. Joseph's County.



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Meridian has prepared a referral information kit detailing our facilities and services. In it you will find information on how you and your patients' families in the northern Indiana areas served by our eight facilities can take advantage of the many nursing care programs that we offer. This kit is available, without charge, to physicians and hospital administrations. To obtain a copy for your office, please clip and send the coupon below.

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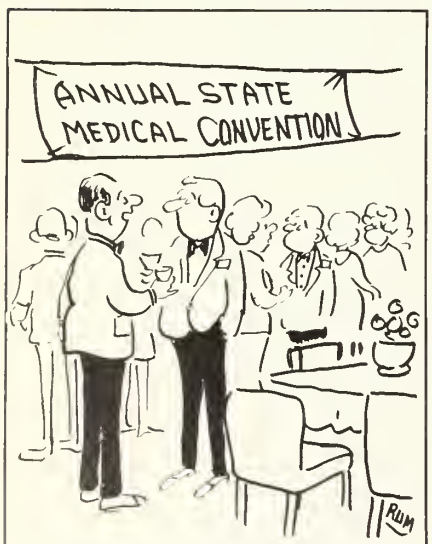
WHAT'S NEW?

News of what is new in the medical supply industry is composed of abstracts from news releases by book publishers and manufacturers of pharmaceuticals, clinical laboratory supplies, instruments and surgical appliances. Each item is published as news and does not necessarily constitute an endorsement of a product or recommendation for its use by INDIANA MEDICINE or by the Indiana State Medical Association.

Rutgers University Press announces release of two new volumes in *Series in Psycholosocial Epidemiology.* All seven volumes in the series are now available: *Ethical Issues in Epidemiologic Research, Community Surveys of Psychiatry, Studies on Children, Stressful Life Events, Symptoms, Illness Behavior, and Help-Seeking, Alcohol Patterns and Problems,* and *Studying Drug Abuse* are available as single volumes or as an entire series, or in any combination.

Abbott Laboratories will market an ambulatory medication infusion pump manufactured by Peter Hannifin Corporation. The programmable electronic infusion device will be used to provide drugs to patients being treated for cancer, pain, or infectious diseases. Such administration of drugs will allow the continuous administration to be on an out-patient basis most of the time, and thus reduce hospital costs.

The Gould/Trinity HAS™ (Hemodynamic Analysis System) combines Gould's expertise in cath lab recording and Trinity Computing Systems' proven expertise in hemodynamic analysis software. The combination provides an integrated system that reduces clerical input time while maintaining a high level of data integrity.



"Boy! The traffic was Beeper-to-Beeper today!"

Midmark Corporation has new, stylish modular cabinets, designed to compliment the Midmark examination tables and ancillary products. Made of extra-heavy welded furniture steel, there are six 25″ wide base units, offering a wide choice of door and/or drawer combinations, two matching corner units and one 14″ wide base unit plus a one or two drawer desk.

The **Lanier Business Systems** Division of Harris Corporation announces Concept 6300, an enhancement of its line of office automation systems for the medical profession. Users may attach up to eight personal computer workstations to Lanier's 6000 workgroup server. Concept 6300 provides low-cost networking to users who require both Lanier propietary and IBM-compatible PC workstations.

Roche announces FDA approval of labeling of alpha tocopherol, a form of vitamin E, to the surface of bacon to prevent the formation of potentially harmful chemical compounds called nitrosamines that are produced during frying. This is a result of a 10-year research effort by Hoffmann-La Roche, a portion of it in cooperation with the Agricultural Department.

Allscrips Pharmaceuticals has developed a new system of in-office dispensing that offers the physician and his patients maximum benefits with minimum investment in time, effort, and dollars. Physicians may order their own custom formulary, which is supplied by Allscrips in pre-packaged prescription-sized, tamper-evident containers along with complete labeling.

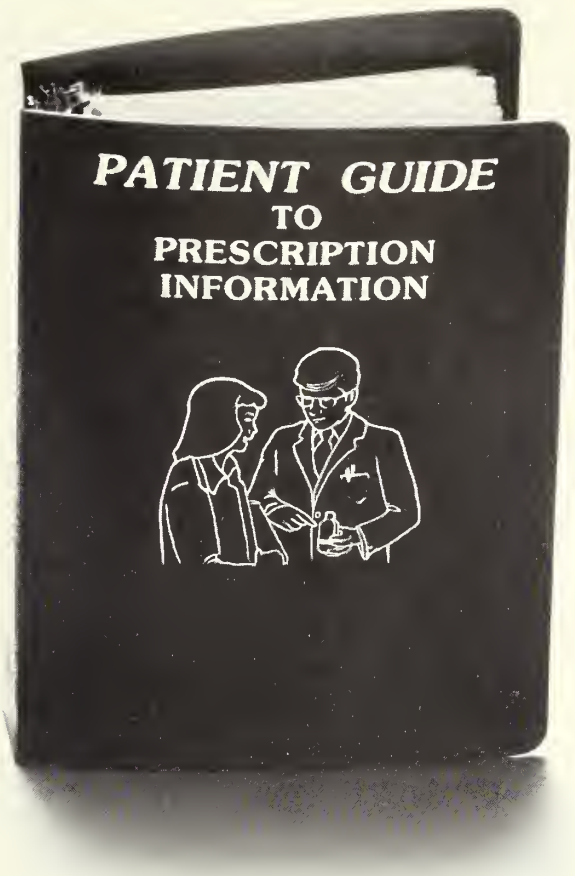
Hewlett-Packard has a new patient-information review station, HP CareView, which facilitates rapid decision-making and tracking of patient status. The system uses the HP Vectra personal computer with touch-sensitive screen. CareView (78730) provides a "window" to the HP Care-Net critical-care network of patient-monitoring equipment, enabling patient assessment from remote locations.

Western Enterprises announces a fill and transfer hose designed for cryogenic liquid oxygen and nitrogen. Maximum working pressure is 1000 psig. The hose is made in various lengths from 48″ to 144″ and has an internal diameter of 1/2″. If required, a Cryogenic Hose Elbow is available, as well as Western's Cryogenic Phase Separator, which increases filling speed while reducing splashes.

Hewlett-Packard has a new HP 43200A monitor-recorder, a lightweight battery- and line-operated unit suitable for use as a cardiac monitor in emergency rooms and for transport monitoring within the hospital. Using the same design, packaging and electronics as the HP 43100A defibrillators, the new monitor/recorder (which has no defibrillator) can tie into the HP 78560A central station to provide a simple, inexpensive central-monitoring solution.



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Every Peoples has an unlisted phone that's reserved only for doctors and answered only by pharmacists. Please call your local store to obtain the number.

PEOPLES DRUG

FUTURE FILE

Family Practice

The Twelfth Annual Family Practice Symposium will be held on April 29-30 at the Crown Center Hotel in Kansas City, Missouri. Credits in unspecified amounts are allowed for AMA and AAFP.

The correspondent is Eileen Buttron, Office of CME, 39th and Rainbow Blvd., Kansas City, Kansas 66103—(913) 588-4494.

Minhas Lectureship

The Kareem B. Minhas Memorial Lectureship will be held Friday, March 27, at 8 a.m. in the second floor auditorium, Kosair-Children's Hospital, Louisville, Ky.

Arthur Garson Jr., M.D., Professor of Pediatrics and Medicine, Baylor College of Medicine, will speak on "The Normal Child with Irregular Heartbeat." Sponsored by the University of Louisville. One hour of Category 1 credit.

For information, call (502) 562-8816.

Infectious Diseases

"Advances in the Management of Infectious Diseases" is the title of a CME course of the University of Michigan Medical School to be held at the Kahala Hilton in Honolulu on February 19-21. Eleven and 75/100 credits are allowed by Category 1 of the AMA and the Michigan Academy of AAFP. The fee is $285.

The correspondent is Gayle Fox, Office of CME, Towsley Center, Box 0201, Ann Arbor, Michigan 48109—(313) 763-1400.

Clinical Conference

"Practical Solutions to Practice Problems: Clinical Medicine in Practice" is the title of the 43rd Annual Midwest Clinical Conference which meets on March 6, 7 and 8 at the Chicago Hilton and Towers. Category 1 credits are up to 20 hours.

Write or phone the Chicago Medical Society, 515 N. Dearborn St., Chicago 60610—(312) 670-2550.

Medical Education

"How Can We Increase the Role of the Ambulatory Setting in Medical Education? Are HMOs the Answer?" is the subject of an all-day meeting at the New York Hilton, New York City, on February 19.

The program is co-sponsored by the Long Island Jewish Medical Center. The tuition is $150. Hospital directors, general internal medicine program chiefs, HMO medical directors and deans of medical schools are the expected audience.

The address of the Medical Center is New Hyde Park, New York 11042.

Indiana University CME

Feb. 19: Update in Infectious Diseases, Reid Memorial Hospital, Richmond.

Feb. 21-22: Annual Meeting, Indiana Society of Anesthesiologists and Anesthesia Update, Radisson Hotel, Indianapolis.

March 3-4: Pediatric Critical Care in Perspective, Sheraton Meridian, Indianapolis.

March 5: General Principles of Oncology, Reid Memorial Hospital, Richmond.

March 18: Dermatology Update for the Non-Dermatologist, Sheraton Marten House, Indianapolis.

March 20: Clinical Aspects of Immunosuppressive Therapy in Multiple Sclerosis, Embassy Suites-Downtown, Indianapolis.

March 20: Hard of Hearing Child, Myers Auditorium, Wishard Memorial Hospital, Indianapolis.

For further information on these and other CME programs contact Melody Dian, Assistant Director, CME, I.U. School of Medicine—(317) 274-8353.

The *Journal of the American Medical Association* publishes a list of CME courses for the United States twice yearly. The January listing features courses offered from March through August; the July listing features courses offered from September through February.

Methodist Hospital CME

Jan. 28: Managing Hypercholesterolemia: New Technologies and Treatment Guidelines, Methodist Hospital, Indianapolis.

Feb. 13-16: 3rd Annual M.H. Perinatology Symposium, Americana Resort, Lake Geneva, Wisc.

Feb. 19-20: Cancer Management Course (co-sponsored by American College of Surgeons), Methodist Hospital auditorium.

Feb. 28-March 1: 3rd Annual Symposium on Extracorporeal Shock Wave Lithotripsy, Hilton on the Circle, Indianapolis.

March 13-14: Advanced Trauma Life Support, Methodist Hospital.

For more information, contact Dixie Estridge, CME coordinator, Graduate Medical Center, Methodist Hospital of Indiana—(317) 929-3733.

Kentucky CME Offerings

The University of Kentucky at Lexington will conduct CME courses as follows:

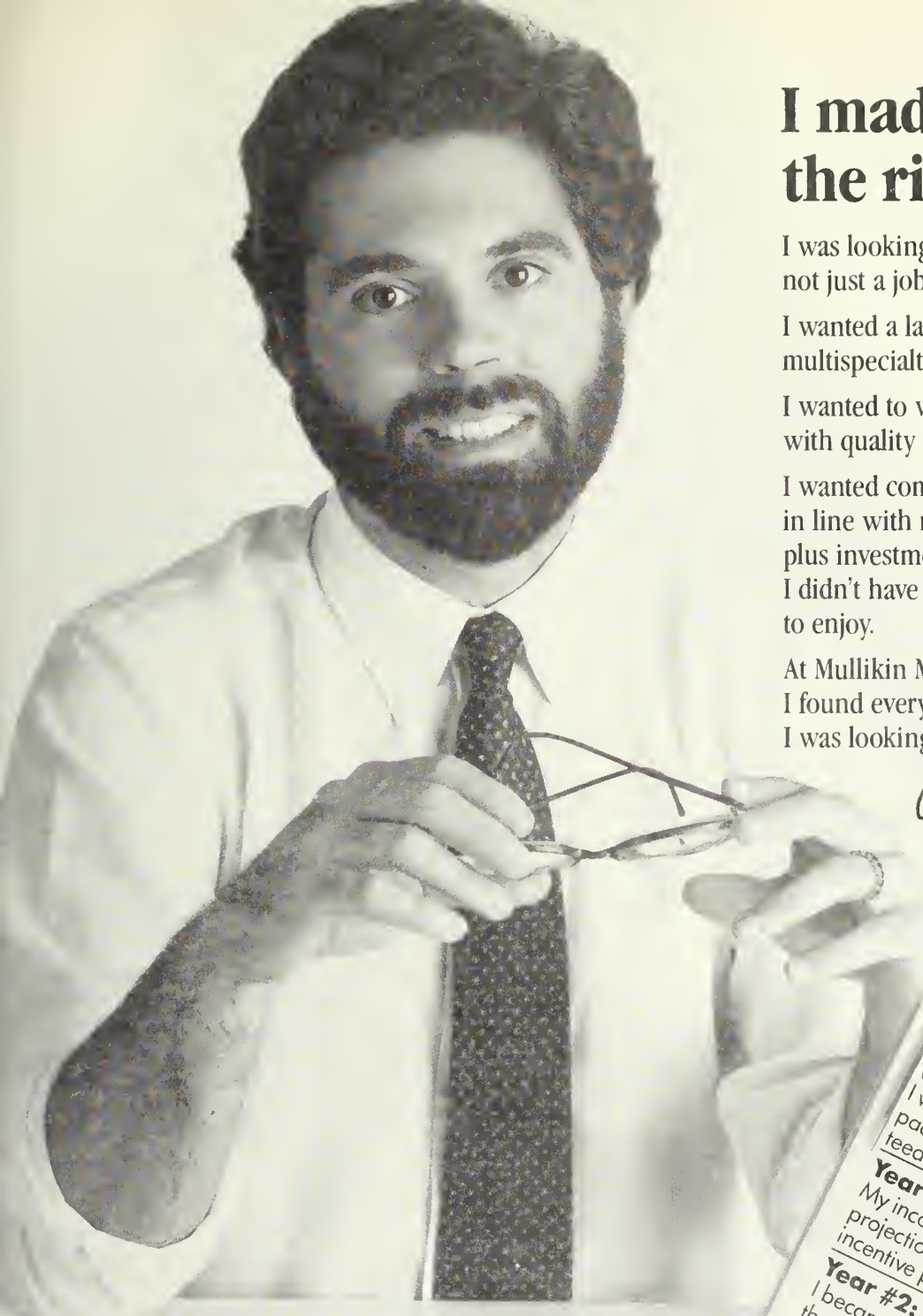
"Hypertension: New Directions" on April 10 and 11; "Contact Lens Workshop" on April 10 to 12; "Contemporary Pediatrics for the Practicing Physician" on April 24 and 25; and "Eighteenth Family Medicine Review—Session II, May 17 to 22. All at the Hyatt Regency Hotel in Lexington. All courses are accredited under Category 1 for the AMA.

The correspondent is Joy Greene, CME, 112 College of Medicine Office Building, Lexington, Ky. 50536—(616) 233-5161.

Kansas CME Course

"Anticoagulant and Antithrombotic Therapy: State of the Art" is the title of a CME course to be presented on April 25 at the Alameda Plaza Hotel, Kansas City, Kansas 66103. Credit for Category 1 AMA, AAFP and CNE.

The correspondent is Eileen Buttron, Office of CME, 39th and Rainbow Blvd., Kansas City, Kansas 66103—(913) 588-4480.



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CANCER CORNER

WILLIAM M. DUGAN, JR., M.D.
Methodist Hospital Cancer Care Center, Indianapolis

ESTATES: PLANNING AHEAD, is a new booklet published by the Northern California Cancer Program. The book is divided into three sections: general estate planning, funeral planning and tissue and organ donations. There is also a Health Professional supplement that includes additional details regarding tissue and organ donations. This free booklet can be obtained from the Northern California Cancer Program, 1301 Shoreway Road, Suite 245, Belmont, Calif. 94002.

THE CANCER PATIENT'S HANDBOOK is now available through COPE magazine for people who work with cancer patients, friends and family of cancer patients and for cancer patients. The book is based on proven practices at major medical centers and tells you how to choose the right doctor and treatment center, questions to ask at every step of diagnosis and treatment, pros and cons of surgery, radiation therapy and chemotherapy, the latest on minimized side effects, managing pain, nutrition and diet and how to handle emotional setbacks and stress. The handbook also includes an extensive glossary, an annotated list of books, booklets, audio cassettes, and a directory of organizations providing community and regional support.

Hardcover handbooks are $24.95 each and paperback handbooks are $14.95 each, not including $1.75 for postage and handling. To order send your check to COPE magazine, Suite B-400, 12600 W. Colfax, Denver, Colo.

FOR CANCER PATIENTS that want to learn more about living with cancer dial 1-800-343-COPE, a service of COPE Magazine.

ADVANCES IN DIAGNOSING AND TREATING LUNG CANCER will be the program topic at the Columbus Cancer Conference on March 6, 1987. The full day accreditated seminar will be held at the Hyatt on Capitol Square in Columbus, Ohio and will feature presentations by physicians nationally known in their particular fields. Registration deadline is February 20, 1987. For further information contact Angie Leonard, Regional Cancer Institute at Riverside Methodist Hospital, 3535 Olentangy River Road, Columbus, Ohio 43214.

1986-87 PROFESSIONAL EDUCATION MATERIALS CATALOG is available through the American Cancer Society. The audio-visual and printed materials are provided to physicians, dentists, nurses, and other professionals for the purpose of continuing education. For more information regarding available materials contact the Medical Affairs Department, American Cancer Society, Indiana Division Inc., 9575 N. Valparaiso Court, Indianapolis 46268.

MARCH CONFERENCES: 5th International Conference on the Adjuvant Therapy of Cancer sponsored by the Arizona Cancer Center at Tucson, Ariz., will be held March 11-14. For further information contact: Mary Humphrey, Conference Coordinator, Arizona Cancer Center, University of Arizona College of Medicine, Tucson, Ariz. 85724 or call 602/626-6044.

The Third National Symposium of the Leukemia Society of America will be held March 18-21 in San Diego; it is sponsored by the Leukemia Society of America. For further information contact Alfred Van Horn III, Conference Manager, LSA Medical Conference, c/o Bostrom Management Corporation, 435 North Michigan, Chicago 60611 or call 312/644-0828.

COPING WITH CHEMOTHERAPY is a book that has everything you need to know about chemotherapy including: how chemotherapy works, how to decide if it's right for you, treatment options, support for mind, body and spirit, diet nutrition, exercise, drugs and their side effects, how to make the most of patient-doctor relationships and the emotional aspects. The book is $15.95 plus $1.94 for handling and can be obtained by writing COPE magazine, Suite B-400, 12600 W. Colfax, Denver, Colo. 80215.

QUIT SMOKING. Fresh Start Quit Smoking Clinics will be held on: February 14, March 9, 12, 16, 19, April 11, June 13, July 13, 16, 20, 23, September 12, 1987. For further information and registration contact your local American Cancer Society.

4th ANNUAL ADVANCES IN CANCER TREATMENT RESEARCH SYMPOSIUM, sponsored by Montefiore Medical Center, will be held March 26-27, 1987 at The Grand Hyatt in New York City.

The main topics include: Hematologic Issues in Oncology, Clinical Investigations in Solid Tumors, New Approaches in Oncology, and Investigation for the Future. Lectures are accredited by The Cancer Research Center of the Albert Einstein College of Medicine.

For general information regarding tuition and accommodations call the office of Continuing Education at 212/920-6674 or write to Albert Einstein College of Medicine, Office of Continuing Education, Montefiore Medical Center, 3301 Bainbridge Ave., Bronx, N.Y. 10467.

FEBRUARY CONFERENCES: Oncology Practice 1987: A Perspective, Sponsored by the Baylor University Medical Center, at Snowmass, Colorado, February 1-7, 1987. For further information contact: Stephen E. Jones, M.D., Samons Cancer Center #4800, Baylor University Medical Center, 3500 Gaston Ave., Dallas, Tex. 75246.

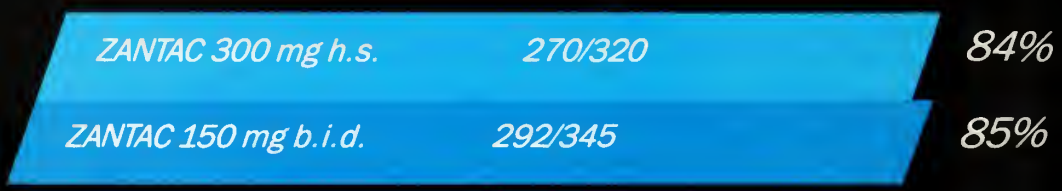
The 35th Annual Meeting of the Radiation Research Society, sponsored by the Radiation Research Society, will be conducted Feb. 22-26 at Atlanta. Inquiries should be made to: Radiation Research Society, 925 Chestnut Street, Philadelphia, Pa. 19107 or call 215/574-3153.


CONTROL
ACID RAIN
with once-a-night
h.s. therapy for active
duodenal ulcers

Only one tablet at bedtime

Controls nocturnal acid to relieve pain and heal duodenal ulcers

Heals active duodenal ulcers after 4 weeks in most patients*[1]



In well-controlled, double-blind, multicenter trials, ZANTAC 300 mg h.s. healed active duodenal ulcers in 84% of patients after 4 weeks. After 8 weeks, healing rates may be higher with ZANTAC 150 mg b.i.d. (92%) than with ZANTAC 300 mg h.s. (87%).

Relieves pain and other symptoms as effectively as ZANTAC 150 mg b.i.d.[1]

Zantac® 300

ranitidine HCl/Glaxo 300 mg tablets

Once-daily dosing may enhance compliance in patients for whom dosing convenience is important

Side-effects profile comparable to ZANTAC 150 mg b.i.d.[1-3]

Headache—sometimes severe—has been reported. Rare effects on the CNS, cardiovascular, GI, hepatic, and integumental systems have been observed, as well as rare cases of hypersensitivity reactions. See ADVERSE REACTIONS section of Brief Summary of Product Information before prescribing.

No significant interference with the hepatic cytochrome P-450 enzyme system at recommended doses

ZANTAC 300 mg h.s. had no significant drug interactions with theophylline or warfarin. The bioavailability of certain medications whose absorption is dependent on a low gastric pH may be altered when ZANTAC or other medications which decrease gastric acidity are administered.



*It is not known exactly how much acid inhibition is needed to heal ulcers.

Glaxo / ROCHE

See next page for references and Brief Summary of Product Information.

IN ACTIVE DUODENAL ULCERS

Once-a-night h.s. therapy controls acid rain

Zantac® 300
ranitidine HCl/Glaxo 300 mg tablets

References: 1. Data available on request, Glaxo Inc. **2.** Ireland A, Colin-Jones DG, Gear P, et al: Ranitidine 150 mg twice daily vs 300 mg nightly in treatment of duodenal ulcers. *Lancet* 1984;2:274-275. **3.** Colin-Jones DG, Ireland A, Gear P, et al: Reducing overnight secretion of acid to heal duodenal ulcers. *Am J Med* 1984; 77 (suppl 5B):116-122.

ZANTAC® 150 Tablets
(ranitidine hydrochloride)
ZANTAC® 300 Tablets
(ranitidine hydrochloride)

BRIEF SUMMARY OF PRODUCT INFORMATION

See complete product information before prescribing. The following is a brief summary.

INDICATIONS AND USAGE: ZANTAC® is indicated in:
1. Short-term treatment of **active duodenal ulcer**. Most patients heal within four weeks.
2. **Maintenance therapy** for duodenal ulcer patients at reduced dosage after healing of acute ulcers.
3. The treatment of **pathological hypersecretory conditions** (eg, Zollinger-Ellison syndrome and systemic mastocytosis).
4. Short-term treatment of **active, benign gastric ulcer**. Most patients heal within six weeks and the usefulness of further treatment has not been demonstrated.
5. Treatment of **gastroesophageal reflux disease (GERD)**. Symptomatic relief commonly occurs within one or two weeks after starting therapy. Therapy for longer than six weeks has not been studied.

In active duodenal ulcer; active, benign gastric ulcer, hypersecretory states; and GERD, concomitant antacids should be given as needed for relief of pain.

CONTRAINDICATIONS: ZANTAC® is contraindicated for patients known to have hypersensitivity to the drug.

PRECAUTIONS: General: 1. Symptomatic response to ZANTAC® therapy does not preclude the presence of gastric malignancy. 2. Since ZANTAC is excreted primarily by the kidney, dosage should be adjusted in patients with impaired renal function. Caution should be observed in patients with hepatic dysfunction since ZANTAC is metabolized in the liver.

Laboratory Tests: False-positive tests for urine protein with Multistix® may occur during ZANTAC therapy, and therefore testing with sulfosalicylic acid is recommended.

Drug Interactions: Although ZANTAC has been reported to bind weakly to cytochrome P-450 in vitro, recommended doses of the drug do not inhibit the action of the cytochrome P-450-linked oxygenase enzymes in the liver. However, there have been isolated reports of drug interactions which suggest that ZANTAC may affect the bioavailability of certain drugs by some mechanism as yet unidentified (eg, a pH-dependent effect on absorption or a change in volume of distribution).

Carcinogenesis, Mutagenesis, Impairment of Fertility: There was no indication of tumorigenic or carcinogenic effects in lifespan studies in mice and rats at doses up to 2,000 mg/kg/day.

Ranitidine was not mutagenic in standard bacterial tests (*Salmonella, E coli*) for mutagenicity at concentrations up to the maximum recommended for these assays.

In a dominant lethal assay, a single oral dose of 1,000 mg/kg to male rats was without effect on the outcome of two matings per week for the next nine weeks.

Pregnancy: *Teratogenic Effects: Pregnancy Category B:* Reproduction studies have been performed in rats and rabbits at doses up to 160 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to ZANTAC. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: ZANTAC is secreted in human milk. Caution should be exercised when ZANTAC is administered to a nursing mother.

Pediatric Use: Safety and effectiveness in children have not been established.

Use in Elderly Patients: Ulcer healing rates in elderly patients (65 to 82 years of age) were no different from those in younger age groups. The incidence rates for adverse events and laboratory abnormalities were also not different from those seen in other age groups.

ADVERSE REACTIONS: The following have been reported as events in clinical trials or in the routine management of patients treated with oral ZANTAC®. The relationship to ZANTAC therapy has been unclear in many cases. Headache, sometimes severe, seems to be related to ZANTAC administration.

Central Nervous System: Rarely, malaise, dizziness, somnolence, insomnia, and vertigo. Rare cases of reversible mental confusion, agitation, depression, and hallucinations have been reported, predominantly in severely ill elderly patients.

Cardiovascular: Rare reports of tachycardia, bradycardia, and premature ventricular beats.

Gastrointestinal: Constipation, diarrhea, nausea/vomiting, and abdominal discomfort/pain.

Hepatic: In normal volunteers, SGPT values were increased to at least twice the pretreatment levels in 6 of 12 subjects receiving 100 mg qid IV for seven days, and in 4 of 24 subjects receiving 50 mg qid IV for five days. With oral administration there have been occasional reports of reversible hepatitis, hepatocellular or hepatocanalicular or mixed, with or without jaundice.

Musculoskeletal: Rare reports of arthralgias.

Hematologic: Rare reports of reversible leukopenia, granulocytopenia, thrombocytopenia, and pancytopenia.

Endocrine: Controlled studies in animals and man have shown no stimulation of any pituitary hormone by ZANTAC and no antiandrogenic activity, and cimetidine-induced gynecomastia and impotence in hypersecretory patients have resolved when ZANTAC has been substituted. However, occasional cases of gynecomastia, impotence, and loss of libido have been reported in male patients receiving ZANTAC, but the incidence did not differ from that in the general population.

Integumental: Rash, including rare cases suggestive of mild erythema multiforme, and, rarely, alopecia.

Other: Rare cases of hypersensitivity reactions (eg, bronchospasm, fever, rash, eosinophilia) and small increases in serum creatinine.

DOSAGE AND ADMINISTRATION: Active Duodenal Ulcer: The current recommended adult oral dosage is 150 mg twice daily. An alternate dosage of 300 mg once daily at bedtime can be used for patients in whom dosing convenience is important. The advantages of one treatment regimen compared to the other in a particular patient population have yet to be demonstrated.

Maintenance Therapy: The current recommended adult oral dosage is 150 mg at bedtime.

Pathological Hypersecretory Conditions (such as Zollinger-Ellison Syndrome): The current recommended adult oral dosage is 150 mg twice a day. In some patients it may be necessary to administer ZANTAC® 150-mg doses more frequently. Doses should be adjusted to individual patient needs, and should continue as long as clinically indicated. Doses up to 6 g/day have been employed in patients with severe disease.

Benign Gastric Ulcer: The current recommended adult oral dosage is 150 mg twice a day.

GERD: The current recommended adult oral dosage is 150 mg twice a day.

See full prescribing information for dosage adjustment for patients with impaired renal function.

HOW SUPPLIED: ZANTAC® 300 Tablets (ranitidine hydrochloride equivalent to 300 mg of ranitidine) are yellow, capsule-shaped tablets embossed with "ZANTAC 300" on one side and "Glaxo" on the other. They are available in bottles of 30 (NDC 0173-0393-40) and unit dose packs of 100 tablets (NDC 0173-0393-47).

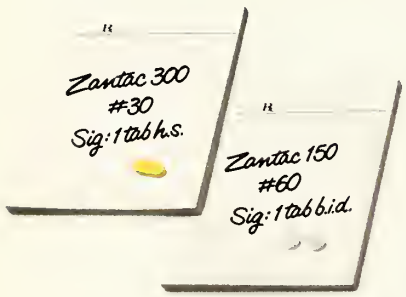
ZANTAC® 150 Tablets (ranitidine hydrochloride equivalent to 150 mg of ranitidine) are white tablets embossed with "ZANTAC 150" on one side and "Glaxo" on the other. They are available in bottles of 60 tablets (NDC 0173-0344-42) and unit dose packs of 100 tablets (NDC 0173-0344-47).

Store between 15° and 30°C (59° and 86°F) in a dry place. Protect from light. Replace cap securely after each opening.

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Glaxo
Glaxo Inc
Research Triangle Park, NC 27709

Two effective regimens to treat active duodenal ulcers:



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Fluid and Electrolyte Disturbances in the Perioperative Period

CRAIG M. STOOPS, M.D.
Indianapolis

DISTURBANCES OF fluids and electrolytes in the perioperative period cause multiple organ system dysfunction with important surgical and anesthetic implications. Electrolytes frequently involved are potassium, calcium and magnesium, as well as imbalances of sodium and water. Knowledge of the pathophysiology of these disorders, their causes and appropriate management can help minimize perioperative morbidity and mortality and hasten recovery.

This review focuses first upon disturbances of electrolyte composition and then upon alterations of volume status involving sodium and water. Both surgical and anesthetic implications of these disorders are discussed. For potassium, calcium and magnesium, a brief physiology review is followed by a discussion of changes in electrolyte composition and the etiologies. Adverse effects on target organs, important anesthetic implications and clinical management are mentioned. Sodium and water balance is the final topic, covered in a similar format. This outline should serve as a quick review of common water and electrolyte changes affecting the surgical patient.

The author is an Assistant Professor of Anesthesia, Indiana University School of Medicine, Indianapolis.

Disturbances of Electrolyte Composition

POTASSIUM

The electrolyte of most importance in the perioperative period is probably potassium. It is the potassium gradient across myocardial cells which determines the resting membrane potential. Cardiac phase 4 depolarization results from intracellular potassium accumulation as its conductance decreases. While the action potential is generated by the sudden influx of sodium and calcium, repolarization involves the egress of potassium from cardiac cells. Although potassium abnormalities are most detrimental to the heart, they also adversely affect the kidney, the gastrointestinal tract and skeletal muscle.

Potassium is readily available in the diet and is almost completely absorbed by the ileum. About 98% of total body potassium is distributed intracellularly, mainly in skeletal muscle. Excess potassium is excreted by the kidney. There is an obligatory daily loss of 20 mEq even in the face of potassium depletion. Renal potassium excretion

is proportional to the urinary output.

Factors which affect potassium homeostasis are primarily humoral. Aldosterone-dependent renal excretion is directly proportional to the serum potassium concentration, independent of renin levels and sodium balance. Potassium is exchanged for either sodium or hydrogen ion in the distal convoluted tubule. Aldosterone also enhances cellular uptake of potassium, the so-called extrarenal effect. Other extrarenal mechanisms alter potassium distribution.

Activation of the sympathetic nervous system moves potassium intracellularly in exchange for sodium via membrane-bound ATPase. Changes in acid-base status, whether respiratory or metabolic in origin, cause redistribution of potassium across cell membranes. A sudden decrease in the serum potassium concentration triggers the release of insulin which drives potassium intracellularly independent of glucose uptake. However, exogenous insulin minimally reduces the serum potassium concentration.

There are pitfalls in using the serum potassium concentration to measure total body potassium stores. This relationship can best be described as a scattergram.[1] For example, as extracellular potassium is lost for some pathophysiologic reason, it is replaced by potassium from within the cells; therefore, the magnitude of total body potassium depletion is underestimated. A chronic reduction in the serum potassium concentration of 1.0 mEq/l reflects a total body deficit of 600 to 1000 mEq.[2] Nonetheless, the serum potassium concentration is the only practical means of assessing total body potassium, even though 98% is located intracellularly.

HYPOKALEMIA

There are both acute and chronic causes of hypokalemia. Chronic total body depletion of potassium reflects either inadequate intake or excessive losses. Oral intake may be inadequate in states of malnutrition. Likewise, there may be insufficient intravenous replacement of obligatory losses in hospitalized patients. Gastrointestinal losses occur through vomiting, gastric suction, enteric fistulae, diarrhea and preoperative bowel preparations. Potassium is lost via the kidney in hyperaldosteronism, Cushing's syndrome, metabolic alkalosis, diabetes mellitus, diuretic therapy and trauma.

In metabolic alkalosis there is an exchange of hydrogen ion for potassium in the distal tubule. Hyperglycemia and diuretics increase urine flow and, therefore, potassium excretion. Obligatory postoperative losses amount to 100 mEq of potassium over the first two days. Acutely metabolic or respiratory alkalosis causes intracellular translocation without any change in total body potassium content. Intraoperative hyperventilation of the lungs and overzealous administration of sodium bicarbonate are the principal culprits. Acute transcellular shifts are rarely important unless super-imposed upon chronic depletion. Furthermore, chronic losses, i.e., hypokalemia secondary to diuretic therapy, are much better tolerated than are acute losses, such as those that occur with vomiting and diarrhea, for example.

The most important target organ of hypokalemia is the heart. Myocardial contractility is impaired. Conduction anomalies associated with increased automaticity result in tachydysrhythmias and ventricular ectopy, especially in patients receiving digitalis and diuretic therapy. An autonomic neuropathy also may adversely affect the heart. Because of loss of the transmembrane gradient, skeletal muscle weakness and degeneration ensue. The consequences are hypoventilation and sometimes myoglobinuria.

Besides this pigment-induced nephropathy, hypokalemia causes renal tubular degeneration, which results in loss of antidiuretic hormone (ADH) responsiveness and concentrating ability with polyuria. Effects on the gastrointestinal tract include ileus and dilatation.

A careful history is necessary preoperatively to elicit conditions associated with chronic hypokalemia. Patients receiving digitalis and diuretics require serum electrolyte determinations. Cardiac rhythm and conduction are evaluated by the electrocardiogram. A histamine-2 receptor antagonist (cimetidine, ranitidine) may be prescribed for prophylaxis against aspiration pneumonitis. Intraoperatively, mechanical hyperventilation of the lungs would superimpose acute shifts upon chronic depletion and must be avoided. Exogenous glucose would induce an osmotic loss of potassium as well as insulin-induced cellular uptake. Dysrhythmogenic drugs, such as halothane, the anticholinergics, pancuronium, gallamine, ketamine, and meperidine, are best avoided.

Autonomic neuropathy and cardiomyopathy dictate judicious use of the cardiodepressant volatile drugs. The neuromuscular blockers may be potentiated by acute intracellular shifts of potassium, although this effect is of minimal clinical significance. Adequate fluid replacement counteracts hypovolemia from preoperative diuretics, polyuria and ADH resistance. Postoperatively, respiratory muscle strength must be carefully assessed prior to tracheal extubation.

Acute intracellular translocation of potassium is easily avoided by preventing its cause, metabolic or respiratory alkalosis. Chronic total body deficits are corrected by potassium chloride supplementation, 0.2 to 0.5 mEq/kg/hr not to exceed 240 mEq/day intravenously, or orally 25 mEq qid for a week. The latter is safer, more effective, and avoids the problems of pain, phlebitis and inadvertent hyperkalemia with serious dysrhythmias. Unfortunately, most of the administered potassium is excreted by the kidney, especially if the underlying etiology of potassium loss cannot be corrected.[3] There is evidence, however, that even partial restoration of a total body potassium deficit helps normalize

electrophysiology and provides an antidysrhythmic effect against digitalis.

The acceptable lower limit of serum potassium concentration for elective surgery is undefined. Without scientific basis, it has generally been quoted as 3.0 mEq/1. While chronic hypokalemia and acute intracellular shifts are generally well tolerated, acute losses are more dangerous because of abnormal transcellular gradients.

A recent study reports that moderate chronic hypokalemia (serum [K] 2.6 to 3.4 mEq/1) is not associated with an increased incidence of intraoperative dysrhythmias.[4] These authors challenge the practice of delaying surgery until potassium stores are totally or even partially repleted in asymptomatic chronically hypokalemic patients. Their data do not, however, establish a safe lower limit. Furthermore, the results may not apply in the face of coronary artery disease, digitalis therapy or a history of serious cardiac dysrhythmias. A universal conclusion is that the entire clinical situation must be assessed to determine the significance of a single preoperative potassium value.[5,6] Intraoperatively, acute reductions in serum potassium concentration should not be superimposed upon pre-existing chronic hypokalemia.

HYPERKALEMIA

Hyperkalemia results from a total body overload or extracellular redistribution of potassium. Chronic renal failure is associated with decreased excretion of potassium. In Addison's disease, hypoaldosteronism, and metabolic acidosis, potassium is reabsorbed by the kidney in exchange for sodium or hydrogen ion. Iatrogenic causes of hyperkalemia include the administration of "potassium-sparing" diuretics, old banked blood, and the potassium salt of penicillin. There may be inadequate mixing of potassium and intravenous fluids in plastic containers with potassium settling to the bottom to be infused as a bolus.[7] Extracellular redistribution of potassium occurs with metabolic or respiratory acidosis, chemotherapeutic cell lysis, hemolysis, tissue ischemia and diabetes. The classic example of extracellular redistribution is succinylcholine-induced hyperkalemia in spinal cord transection, neurologic disease, burns and crush injuries.

Myocardial contractility is impaired in hyperkalemia. Conduction and automaticity are decreased, resulting in heart block, ventricular fibrillation and asystole. Hypoventilation is caused by skeletal muscle weakness. Compensatory hyperaldosteronism leads to sodium and water retention.

Preoperative and postoperative considerations are the same as for hypokalemia. Intraoperatively, dysrhythmogenic drugs, succinylcholine and potassium-containing intravenous solutions should be avoided. Mild hyperventilation of the lungs lowers the serum potassium concentration.

The treatment of hyperkalemia follows three directions. Calcium salts counteract the negative inotropic and chronotropic effects of hyperkalemia. Heart block may be treated electrically with a temporary transvenous pacemaker, if time permits, or chemically with a drug such as isoproterenol in more emergent situations. An intracellular shift of potassium is accomplished with sodium bicarbonate administration, hyperventilation of the lungs and a glucose-insulin infusion. Elimination of potassium is hastened by osmotic and loop diuretics, exchange resins and dialysis.

Akin to the situation with hypokalemia, the acceptable safe upper limit of serum potassium concentration for elective surgery is undefined. The range that is generally quoted without scientific basis is 5.5 to 6.0 mEq/1. Acute hyperkalemia, from an overdose of potassium chloride, for example, is tolerated less well than chronic hypokalemia, as might result from adrenal insufficiency.

CALCIUM

Calcium is involved in membrane function and cellular metabolism. Disturbances in calcium homeostasis, therefore, affect myocardial contractility, conductivity and automaticity, neuromuscular transmission, and skeletal muscle contractility. Its kinetics are complex. Intestinal absorption is dependent upon the active form of vitamin D. Calcitonin causes calcium deposition in bone. Parathyroid hormone regulates skeletal mobilization and renal reabsorption. Intracellularly, calcium combines with a protein called calmodulin. This calcium-calmodulin complex ignites metabolic processes such as those dependent upon the cyclic nucleotides and phosphodiesterases.

It is the ionized fraction of the total serum calcium concentration which is physiologically active and therefore important to quantitate. About 45% of the total serum calcium concentration is ionized, while the rest is either protein-bound or coupled to anions such as bicarbonate, citrate and phosphate. The serum ionized calcium concentration remains normal despite hypoalbuminemia. However, the total serum calcium and albumin concentrations are directly related. The ionized fraction is inversely proportional to the arterial pH.

HYPOCALCEMIA

Hypocalcemia results from either inadequate mobilization of calcium or maldistribution of calcium ion. Vitamin D deficiencies include malabsorption syndromes, bowel resection and inability to activate 1,25-dihydroxycholecalciferol because of renal or hepatic impairment. Hypoparathyroidism may be a primary endocrinopathy or may result from intentional parathyroidectomy or inadvertent parathyroidectomy during thyroidectomy. Ionized calcium is sequestered in pancreatitis. It is bound to anionic sites on plasma proteins in respiratory or metabolic alkalosis. Likewise, rapid infusions of plasma proteins cause transient falls in the serum ionized calcium concentration by the same mechanism. Bind-

ing of ionized calcium to citrate anion in banked blood, so-called citrate intoxication associated with rapid transfusion, is significant only in the neonate, in hypothermic patients, or in patients with liver or kidney disease. Hypoalbuminemia causes a "pseudohypocalcemia," with lowered total serum calcium but normal ionized calcium levels. Calcium entry blockers, while not changing calcium levels per se, do alter function at the cellular level.

Hypocalcemia affects the cardiovascular system and the nervous system. There are negative inotropic, chronotropic and dromotropic effects, as well as systemic and pulmonary vasodilatation. At the neuromuscular junction, less acetylcholine is released presynaptically, resulting in muscle weakness. A sudden reduction in the serum ionized calcium concentration, secondary to acute respiratory alkalosis, for example, causes muscle spasm and tetany. Centrally, the seizure threshold is lowered.

It is important preoperatively to realize that the diagnosis of hypocalcemia depends upon a decreased level of serum ionized calcium. The heart should be examined for evidence of congestive failure. Bradydysrhythmias, as well as other rhythm disturbances and conduction anomalies, are apparent on the preoperative electrocardiogram. The patient receiving calcium entry blocking drugs for coronary artery disease, supraventricular dysrhythmias, systemic or pulmonary hypertension, or cerebral artery vasospasm is, in a sense, "hypocalcemic." Intraoperatively, the potent inhaled drugs must be used judiciously to avoid untoward cardiovascular depression. Neuromuscular blockers must be titrated to a peripheral nerve stimulator. They may be potentiated by certain antibiotics. Metabolic and respiratory alkalosis should be avoided. Rapid infusions of plasma proteins or banked blood bind ionized calcium and lower its serum concentration. Postoperatively, respiratory muscle strength must be carefully assessed along with the adequacy of antagonism of neuromuscular block. Post-thyroidectomy and -parathyroidectomy patients must be carefully observed for signs of airway obstruction secondary to laryngeal tetany, as the intrinsic muscles of the larynx are exquisitely sensitive to hypocalcemia.

Hypocalcemia is treated by correction of the underlying causes and by the administration of calcium salts, orally in chronic situations, and acutely, by the intravenous route. It is important to remember that acute hypocalcemia from citrate intoxication, respiratory alkalosis, or inadvertent or intentional parathyroidectomy is poorly tolerated compared to chronic hypocalcemia resulting from malabsorption.

HYPERCALCEMIA

Causes of hypercalcemia include hyperparathyroidism, renal failure and secondary hyperparathyroidism, bony metastases, immobilization, thiazides, granulomatous disease, and vitamin D intoxication. Organs affected include the cardiovascular system, the kidney and the gastrointestinal system. Hypercalcemia provokes bradydysrhythmias including heart block and hypertension secondary to peripheral vasoconstriction. A diuresis ensues and results in dehydration. There is a progressive azotemia and loss of concentrating ability. Nephrocalcinosis leads to an obstructive nephropathy and eventual renal failure. Gastrointestinal afflictions include pancreatitis, ileus and gastric hyperacidity.

The preoperative blood pressure record must be reviewed and the volume status assessed. Orthostatic changes are anticipated because of hypertension and volume contraction, obligatory diuresis, nausea and vomiting. The electrocardiogram should be reviewed for evidence of bradydysrhythmias. A histamine-2 receptor blocker should be prescribed to raise gastric pH. Induction of anesthesia should be accompanied by aspiration precautions. Adequate volume replacement with sodium-containing fluids is essential, perhaps guided by urinary output and cardiac filling pressures. Cardiodepressant drugs should be carefully titrated, especially in the face of a contracted volume of distribution. With the potential for, at least, subclinical renal impairment, nephrotoxic antibiotics and drugs such as enflurance should be avoided. Neuromuscular blockers should be carefully administered in the face of renal insufficiency, a contracted volume of distribution, and pre-existing skeletal muscle weakness. Postoperatively, both respiratory muscle strength and volume status must be carefully monitored.

The mainstay of treatment of hypercalcemia is rehydration with normal saline and dilution of serum ionized calcium while carefully monitoring other serum electrolyte concentrations, particularly potassium and magnesium. Furosemide inhibits renal reabsorption of calcium. Dialysis also lowers the serum ionized calcium concentration.

MAGNESIUM

Magnesium regulates the presynaptic release of acetylcholine, as an enzymatic co-factor in most high-energy phosphate transfers, and is involved in regulating calcium movement and distribution. It is available in the diet for gastrointestinal absorption. Its distribution is predominantly intracellular. Therefore, like potassium, large total body deficits occur before the serum magnesium concentration is significantly reduced. Depending upon dietary availability, it is either conserved or excreted by the kidney.

HYPOMAGNESEMIA

There are several causes of hypomagnesemia. The most common etiology is chronic ethanol abuse. Hypomagnesemia is a frequent problem in hospitalized patients undergoing parenteral hyperalimentation. Malabsorption syndromes, as well as protracted vomiting and diarrhea, renal tubular damage, diuretic therapy,

hemodialysis, and cardiopulmonary bypass, also lower serum magnesium levels.

The diagnosis of magnesium deficiency requires a high index of suspicion in malnourished patients and measurement of the serum magnesium concentration. The nutritional state and volume status of the afflicted patients must be carefully assessed. Alcoholic complications must be investigated. Intraoperatively, the effects of neuromuscular blocking drugs may be unpredictable. Cardiac rhythm must be carefully monitored. Administration of magnesium salts may aid defibrillation following cardiopulmonary bypass.

The treatment of hypomagnesemia is obviously magnesium sulfate. It should be included in all hyperalimentation regimens and given to alcoholics. Blood pressure, heart rate, and deep tendon reflexes should be monitored during its administration. Complete repletion may require several weeks of therapy.

HYPERMAGNESEMIA

Hypermagnesemia is either caused by renal failure or is iatrogenic in origin. Magnesium is dependent upon glomerular filtration for its excretion. Intake of magnesium is excessive in cases of antacid and laxative abuse. The best known hypermagnesemic patient is the parturient under treatment for toxemia.

Target organs are the neuromuscular junction, the central nervous system, and the cardiovascular system. The release of acetylcholine is inhibited presynaptically by magnesium, resulting in muscle weakness and impaired ventilation. The patient becomes sedated, confused and eventually comatose. There is an anticonvulsant effect of magnesium. Vasodilatation results in hypotension and impaired atrioventricular conduction progresses to heart block.

Pre-, intra-, and postoperatively, intravascular volume must be carefully monitored and replaced. The doses of both depolarizing and nondepolarizing neuromuscular blockers are reduced. The potent inhaled drugs necessitate careful administration because of their vasodilatory properties and the propensity of halothane and even enflurance to slow atrioventricular conduction. Postoperatively, respiratory muscle weakness may necessitate mechanical ventilation of the lungs.

Magnesium intoxication may be antagonized by the administration of calcium. Hydration and diuretics hasten elimination of magnesium. Life-threatening hypermagnesemia requires dialysis.

Disturbances of Volume and Concentration

SODIUM

Sodium abnormalities reflect volume and concentration changes and are unlike other electrolyte disorders which are disturbances of composition. It is impossible, therefore, to discuss sodium balance apart from fluid shifts.

Sodium ion is distributed extracellularly and is involved in the depolarization of nerve, heart and muscle. Dietary intake is unimportant as a source of sodium, because the kidney retains or excretes sodium to adjust water balance. Extracellular fluid volume is carefully defended and conserved primarily by sodium regulation. The quantitation of the serum sodium concentration is really an assessment of the total body water content.

There are a number of factors that affect the kidneys in sodium and water homeostasis. Glomerulotubular balance maintains filtration rate proportional to sodium excretion and, thereby, prevents fluctuations in renal blood flow from altering sodium balance. Hypovolemic states result in redistribution of renal blood flow to the medulla with conservation of sodium and water. Sodium and water retention is also mediated by the renin-angiotensin-aldosterone axis. The existence of a natriuretic hormone has been hypothesized to prevent renal sodium and water reabsorption.

While several mechanisms regulate volume by controlling sodium and water retention or excretion, concentration is regulated by a single process involving ADH. Retention of free water under its influence sometimes maintains volume at the expense of concentration.

HYPERNATREMIA

Hypernatremia is the hallmark of a total body water deficit, although rarely it may reflect a total body sodium excess. In the surgical patient, however, the etiology of hypernatremia is almost always hypovolemia from third-space fluid sequestration, hemorrhage or inadequate replacement of insensible losses. Other causes of hypovolemia, or loss of water in excess of sodium, include fever, burns, the early stages of chronic renal failure, nonoliguric renal failure, and solute-induced diuresis that follows acute tubular necrosis, or may be associated with diabetes mellitus, diabetes insipidus, nephrogenic diabetes insipidus, hyperalimentation, or the use of drugs or radiographic contrast with osmotic properties. Except for end-stage renal disease, most causes of an absolute excess of sodium are iatrogenic: high solute feedings, excessive removal of water with dialysis, steroid excess, hypertonic saline, and sodium bicarbonate therapy.

The target organs of hypernatremia are the cardiovascular and the central nervous systems. Especially with acute hypernatremia, there is cellular dehydration and vascular traction resulting in intracerebral hemorrhage, thrombosis, confusion, coma and convulsions. Chronic hypernatremia is less dangerous to the central nervous system because of the production of "idiogenic osmoles," intracellular solutes that counteract neuronal dehydration. The adverse effects on the cardiovascular system are those of hypovolemia: hypotension, tachycardia, orthostasis, reduced cardiac output with venous and arterial desaturation, prerenal azotemia and oliguria,

myocardial and cerebral ischemia.

The perioperative considerations of hypernatremia are those of hypovolemia. Signs and symptoms are elicited through a careful history and physical examination with heart rate and orthostatic blood pressure determinations. Other useful information includes intake and output balance sheets, along with urinary output, serial weights, hematocrits and serum creatinine determinations. The patient should receive appropriate hydration as time permits. Intraoperatively, vasodilating drugs such as the barbiturates, d-tubocurarine, morphine and the inhaled anesthetics should be avoided or used judiciously. When possible the patient should be positioned to enhance venous return. Positive pressure ventilation of the lungs should be employed cautiously. Blood and fluid replacement must be meticulous. Low-dose dopamine may help to maintain renal perfusion. Preload and urinary output should be monitored along with blood pressure and heart rate. It is important to remember that the pharmacokinetics of both the injected and the inhaled drugs are altered. There is a decreased volume of distribution, and the alveolar concentration rapidly approaches the inspired because of lowered cardiac output. Careful postoperative monitoring of vital signs and volume status is essential.

The treatment of hypernatremia varies with its cause. Chronic hypovolemia is corrected slowly by hypotonic fluid infusion. The osmotic pressure of intracellular idiogenic osmoles may cause cerebral edema during rapid replacement. Guidelines to therapy include vital signs, physical examination, urinary output, cardiac filling pressures, and serum sodium concentration. Acute hypernatremia is treated with rapid free water administration, sometimes in conjunction with diuretics, depending upon volume status. Cerebral edema is not a concern in acute hypernatremia, because time has been insufficient for the production of idiogenic osmoles. Importantly, the underlying cause of hypernatremia should be corrected.

HYPONATREMIA

Hyponatremia may occur with volume contraction (volume loss in excess of water loss), with volume expansion (water retention in excess of sodium retention), or with euvolemia. The causes of hyponatremia are, therefore, exceedingly diverse. Salt may be lost in excess of water with vomiting, diarrhea, gastric suction, third-space losses, osmotic diuresis, mineralocorticoid deficiency, or renal tubular disease. On the other hand, water may be retained in excess of salt in congestive heart failure, cirrhosis, the nephrotic syndrome, and renal failure. Euvolemic hyponatremia is associated with any of the causes of ADH release.

The target organs of hyponatremia are the central nervous system, the neuromuscular junction and the cardiovascular system. The hemodynamic effects depend upon the volume status associated with the hyponatremia. There also are negative inotropic effects, but dysrhythmias are rarely associated with a serum sodium concentration above 100 mEq/1. Intracellular edema of the brain causes intracranial hypertension with confusion, coma and convulsions. The severity of these symptoms is related to the rate of fall of the serum sodium concentration. Hyponatremia causes muscle weakness.

Preoperatively, volume status must be assessed along with an evaluation of cardiac, renal or hepatic disease. Diuretics are administered for hypervolemia. Hypovolemia is treated with appropriate intravenous fluids. Fluid restriction is the treatment for ADH-induced hyponatremia. Intraoperative monitoring of intravascular volume, serum osmolality and electrolytes is essential. Cardiovascular depressants should be employed carefully because of negative inotropy and especially in hypovolemic states. Hyperventilation of the lungs, particularly with enflurane, potentiates central nervous system irritability. Careful titration of neuromuscular blockers is required. Postoperatively, strength of the respiratory muscles must be assessed and the patient protected against aspiration secondary to muscle weakness and a depressed sensorium. Careful monitoring reflects volume status and dictates appropriate therapy.

The treatment of hyponatremia is defined by its etiology, severity and duration. It is more important to evaluate the volume status than to monitor the serum sodium concentration. Sodium-containing solutions are given for hypovolemia, water is restricted for ADH-induced hyponatremia, and hypervolemia is treated with inotropes, diuretics, positive pressure ventilation of the lungs, and positive end-expiratory pressure. Hypertonic saline is effective in severe life-threatening hyponatremia.

Disturbances of Concentration

ANTIDIURETIC HORMONE

The syndrome of inappropriate ADH secretion (SIADH) is an important and common postoperative biochemical change. Its primary etiology is an extracellular fluid derangement secondary to inadequate replacement of perioperative fluid losses. The pituitary-hypothalamic axis releases ADH to increase intravascular volume at the expense of tonicity. Anxiety, pain, surgical stress and anesthetic drugs also cause the inappropriate release of ADH in the perioperative period.

There are a number of conditions that predispose to SIADH besides the stresses of the perioperative period. It is more common with advancing age and with cancer, especially bronchogenic carcinoma. It is often triggered by intracranial pathology. Ethanol withdrawal is another culprit. Postoperative mechanical ventilation of the lungs is another associated condition.

The laboratory findings are those of dilutional hyponatremia. Both serum sodium concentration and osmolality are decreased. Urinary sodium concen-

tration is increased, and there is oliguria.

Prevention is the key to the management of SIADH. Perioperative and especially intraoperative fluid replacement should be generous using a balanced salt solution.

Fluid restriction is the treatment for SIADH that allows increased free water clearance through insensible losses. Sodium administration is useless, as it is excreted immediately in the urine and free water is retained. Life-threatening hyponatremia is treated with furosemide to enhance free water clearance, along with intravenous replacement of urinary sodium and potassium losses.[8]

Disturbances of Concentration and Volume

WATER INTOXICATION

Water intoxication sometimes occurs following transurethral resection of the prostate due to intravascular absorption of hypotonic irrigating fluid. Signs and symptoms are those of fluid overload such as hypertension, bradycardia, and sometimes congestive heart failure. Laboratory studies reveal decreased serum sodium and potassium concentrations, osmolality and hematocrit. Depending upon the severity of the hyponatremia, the patient may become agitated and confused. Intracellular swelling of the brain may cause seizures.

Prevention of this condition during prostatectomy involves limitation of the hydrostatic pressure gradient and short resection times. Once it occurs, water intoxication is treated with inotropes, diuretics and hypertonic saline, so that free water is lost in excess of salt.

Disturbances of Electrolyte Composition

CHLORIDE

Chloride disturbances are similar to sodium derangements, with one important exception: hypochloremic, hypokalemic, metabolic alkalosis. The etiology of this disorder is pernicious vomiting or gastric suction with inadequate replacement. A good example is pyloric stenosis. The treatment is normal saline and potassium supplementation.

Disorders of Electrolyte Composition

LITHIUM

Lithium carbonate is prescribed for the treatment of manic-depressive psychiatric disorders. Lithium mimics sodium by entering excitable cells. However, its removal after depolarization is slow, depressing cellular excitability. The anesthetic implication of this drug is potentiation of both depolarizing and nondepolarizing neuromuscular blocking drugs.

Summary

An understanding of the regulation of electrolyte composition and concentration along with volume status is important in preventing disturbances or in recognizing and correcting them quickly and effectively once they do occur. Perioperative management involves cooperation and careful coordination between the internist, surgeon and anesthesiologist. This review is one approach to solving fluid and electrolyte problems in the surgical patient.

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Primary Cardiac Angiosarcoma with Disseminated Bone and Soft Tissue Metastases

A Reassessment of Diagnostic Criteria Based upon a Review of the Literature

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Abstract

A case of primary cardiac angiosarcoma presenting with symptoms of an acute CNS hemorrhage is described. Current standards for determining the primary or secondary nature of angiosarcomatous lesions of the heart are discussed, with special attention to the criteria proposed by the Armed Forces Institute of Pathology, and examined in regard to cases cited in the world literature. On the basis of recorded metastatic patterns, the current AFIP criteria are challenged, and new recommendations made for the determination of the primary or metastatic nature of angiosarcomas involving the heart.

VARIOUS SITUATIONS in pathology often require that diagnostic criteria be established on the basis of limited data. Often these criteria are arbitrary, reflecting the personal biases of those individuals or centers who have either first described a lesion or observed the largest case load of the particular entity in question. Although such criteria are useful, and often receive confirmatory validation at a later time, occasionally such criteria are found to be not justified when compared to increasing case reports and accumulated data.

Angiosarcoma is a rare malignant neoplasm of endothelial cell derivation. Multiple soft tissue sites have been identified as primary sites, two of the most frequent being bone and heart. Although still an uncommon neoplasm, on the basis of recorded cases it can no longer be considered rare in either of these two sites. Recent personal experience with a case prompted a review of the existing literature, which suggests that the current criteria established by the AFIP regarding determination of primary site, although based on the largest single series of cases, does not reflect the total reported English language literature experience with this neoplasm and therefore can no longer be considered unchallengable.

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Report of the Case

Following initial presentation to the Emergency Department in an awake and alert state, a 47-year-old white man progressed from mild right hemiparesis to a complete comatose state. Radiologic examination showed a large left hemispheric hemorrhagic lesion with midline shift. An incidental radiologic finding was that of a lytic lesion of the left fourth rib. In spite of maximum supportive therapy, the patient died less than 48 hours following admission. On the basis of the lytic rib lesion, an autopsy was ordered.

Multiple unexpected findings were found on autopsy. The fourth rib lesion grossly consisted of a destructive hemorrhagic and necrotic lesion measuring 2 x 2 x 3 cm. Additional bony lesions were not seen. On opening the right atrium, a mass with similar cross section appearances—namely, hemorrhagic and necrotic with loculated and organizing clots—was found which had gross dimensions of 4 x 4 x 5 cm. This was adherent to the atrial septum and appeared to be covered by endocardium. The lesion did not protrude into the tricuspid valve and appeared to cause no obstruction of the right atrial outflow. Multiple nodules, 2 to 3 cm in size, were encountered throughout both lungs in a miliary pattern. A single 2 cm loculated nodule was present in the left lobe of the liver. No additional or cutaneous lesions were seen. On sectioning of the brain following fixation, a larger destructive hemorrhage was seen involving the left frontoparietal lobe with associated transtentorial and transforamenal herniation. Distinct areas of neoplasm could not be

recognized grossly.

Microscopically, the neoplasm was an angiosarcoma. The prominent features were abnormal proliferations of malignant endothelial cells forming freely anastamosing vascular channels, a fine reticulum framework, and foci of alternating solid cellular areas. The individual cells were anaplastic appearing spindled endothelial cells with clear-cut invasive tendencies, most readily identified in sections from rib and heart. Multiple sections from the central nervous system showed remnants of angiosarcoma associated with the left hemispheric hemorrhage and additional foci within the cerebellum and caudate nucleus. Positive Factor VIII associated antigen staining by PAP Immunoperoxidase Method confirmed the endothelial nature of the neoplastic cells. On the basis of the lesion size and hematologic pattern of dissemination, the final impression favored primary right atrial angiosarcoma with metastases to brain, lung, rib and liver.

No history of toxic exposure to vinyl chlorides, thorium dioxide, or potassium arsenite could be elicited from family or friends.

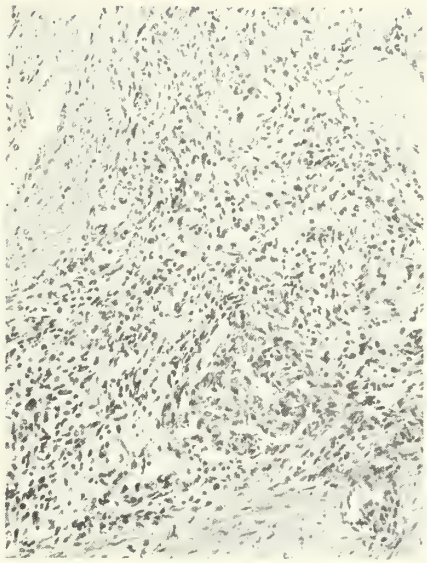


FIGURE 1: Histologic section from metastatic angiosarcoma in lung, H&E. 360X.



FIGURE 2: Histologic section from metastatic angiosarcoma in lung, Reticulin Stain. 360X.

Discussion

Until the recent advent of immunohistochemical staining techniques for the demonstration of specific endothelial tissue antigens, the diagnostic criteria applied to angiosarcomas were those proposed by A. P. Stout in 1943.[53] These included the formation of atypical endothelial cells in group numbers greater than those required to line vessels with a simple endothelial membrane; and secondly, the formation of vascular tubes with a delicate framework of reticulin fibers and a marked tendency for their lumens to anastamose. In differentiating this neoplasm from primary pericytic tumors, Stout advocated the use of silver stains to demonstrate the presence of cells within fine reticular tubes, in contrast to the cells of a pericytoma being outside the vessel wall. Although still valid, the recent development of immunohistochemical techniques to specifically identify endothelial cells has established an entirely new set of criteria for the conclusive diagnosis of this lesion.

The next level of diagnoses pertaining to angiosarcomatous tumors involves assigning the primary site and differentiating this from metastatic deposits. In the Armed Forces Institute of Pathology Fascicle on Tumors of the Cardiovascular System,[36] criteria have been established to include only patients in whom the heart was unequivocally the primary site, specifically those in whom the metastases were small and did not involve the skin or soft tissues. Further clarification of these criteria (personal communication)[45] indicates that in the presence of bone or soft tissue lesion, the cardiac lesion must always be considered a metastatic site. These criteria are based on their series of 34 patients, only 11 of whom demonstrated distant metastases.

A review of the literature revealed a total of 73 previously documented cases of primary angiosarcoma of the heart with an 18% incidence of distant bony metastases.[1,2,17,20,23,26,31,34,36,38,43,45-49,51,55-57,61] A simultaneous review of the English language literature on primary angiosarcomas of the bone reveals 138 cases with no documented metastases to the heart.[3-16,18,19,21,22,24,25,27-30,32,33,35,37,39-42,44,50,52-54,58-60] These statistics are clearly at variance with the AFIP criteria, in that not a single previous literature report confirms the occurrence of metastatic disease in the heart originating from a bone primary. Although this obviously does not preclude other soft tissue sites as being the source of metastatic lesions to the heart, it does raise serious questions as to the validity of the admittedly arbitrary nature of the existing criteria.

Just as the histopathologic criteria for the diagnosis of angiosarcoma has been revised and updated with the advent of new immunohistochemical techniques, a review of the English language literature on primary angiosarcoma of bone and heart origin suggests that previous criteria for the assignment of primary site are no longer entirely valid. The documentation of multiple cases of angiosarcoma

metastasizing from heart to bone, and no single example of the reverse, suggests that simultaneous discovery of both cardiac and bone angiosarcoma does not unequivocally require assignment of the primary site to the bony lesion. Although similar conclusions cannot be drawn regarding other sites of angiosarcoma, the implication is clear that hard-and-fast rules regarding metastatic patterns cannot be relied upon, and clinical judgment of the pathologist reviewing the case is still a vitally important diagnostic tool.

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Idiopathic Enlargement of the Heart, 1895

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In 1895, Dr. Robert Babcock, Professor of the Diseases of the Chest and Clinical Medicine at the College of Physicians and Surgeons in Chicago, accumulated a number of cases of heart disease over a one-year period ending November 1, 1894. Of these, 15.4% were felt to be idiopathic enlargement of the heart. He concluded in the February 1895 issue of the *Western Medical Reporter*, published in Chicago:

"By idiopathic enlargement of the heart is meant combined hypertrophy and dilatation, without valvular disease. The primary condition is not fatty degeneration, which bears no definite relation to the clinical phenomena. The disease results from prolonged high arterial tension, and is observed most frequently in men with large chests and a tendency to corpulence.

"Abnormal arterial tension may arise from excess in food and drink . . . and from severe labor combined with immoderate use of alcohol and tobacco. The diagnosis is not difficult if one remembers that in these large chests actual cardiac enlargement may coexist with a superficial precordial dullness, confined within the so-called normal limits.

"The first indication for treatment is the lessening of the abnormal arterial tension, which is most readily done by means of cathartics and regulation of diet and exercise. Digitalis is harmful, except in cases in which the weakness is confined to the left ventricle. In cases of general cardiac enlargement and weakness, stimulants are called for, such as ammonia, nitroglycerin, ether, valerian, etc.

"The hypodermic injection of 1/10 of a grain of Morphine combined with 1/200 of atropine is the most efficient stimulant in cases suffering from nightly attacks of cardiac asthma. The Schott treatment, by baths and gymnastics, seems specially servicable in this affection before compensation has become irretrievably lost."

At the time of this writing, there were about 8,000 practitioners in the state of Illinois. The *Western Medical Reporter* was one of the major publications of the area. The *Illinois Medical Journal* was officially begun in 1899.

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Psychosomatic Dyspnea

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Abstract

Psychosomatic dyspnea is reviewed. It is quite common and can be considered even during the initial contact with a patient. A thorough evaluation must be done to eliminate an organic cause. Dyspnea occurs in panic attacks, depression, hypochondriasis, and the somatization disorder. Additionally, the sensation of dyspnea or breathlessness may not be congruent with the disease process. Therapy may be difficult and require several modalities of treatment.

THERE ARE SEVERAL definitions of "psychosomatic." The American Psychiatric Association's Psychiatric Glossary defines psychosomatic as the constant and inseparable interaction of the psyche (mind) and soma (body). In the DSM-III, a disorder that in the past would have been referred to as either "psychosomatic" or "psychophysiological" is now diagnosed as "psychological factors affecting physical condition." The Longman Dictionary of Psychology and Psychiatry defines psychosomatic disorder (illness) as a disorder characterized by physical symptoms resulting from psychological factors.

I am using the term psychosomatic in the context that there are no demonstrable organic findings after careful physical examination, appropriate noninvasive or invasive procedures, and evaluation of appropriate laboratory data. In contrast to a factitious symptom or sign and malingering, a psychosomatic sign or symptom is not under voluntary or conscious control.[1] A thorough search must be made for an organic cause of any sign or symptom although the physician can strongly consider a psychosomatic sign or symptom on the first visit. The physician must consider undiagnosed psychiatric disease in medical patients and undiagnosed physical illness manifesting as psychiatric signs or symptoms.[2,3]

Dyspnea, a word frequently used as synonymous with breathlessness, is a totally subjective sensation and cannot be validated by another person. Dyspnea can be considered uncomfortable, difficult, or bothersome breathing that is perceived as a subjective sensation with the modification of the sensation by the interaction of an individual's genetic content and the sum of life experiences.[4]

Psychosomatic dyspnea (breathlessness) is a major problem since the symptom of dyspnea is so very common. During a one-week period, about 40 to 45% of neurotic patients may complain about breathing problems and not getting enough air compared to about 10% of normal subjects.[5] Psychosomatic dyspnea can be part of a somatization disorder[6] or hypochondriasis.[7] Dyspnea is noted in 68 to 100% of patients with anxiety neuroses (or effort syndrome) and in 50 to 75% of patients with the hyperventilation syndrome.[4,8] The hyperventilation syndrome is most congruent with a diagnosis of Panic Disorder.[4] Dyspnea is a major symptom in patients with panic attacks that occur in Panic Disorder, a subtype of Anxiety States (Anxiety Neuroses).[9] Virtually all patients with Panic Disorder will have breathlessness as one of their symptoms when questioned.

Multiple somatic symptoms, including breathlessness, are relatively common in depressive illness. In depressed patients with dyspnea, the dyspnea is episodic, fluctuates within minutes, occurs at rest, bears little relationship to exercise, is emphasized as difficulty getting air in, and the spirogram demonstrates sighing and rapid shallow breathing.[10] A group of patients with unexplained breathing disorder (UBD) was recently described involving 74% of 31 patients with chest pain and normal coronary arteries. The patients with UBD were thought to have significant psychiatric morbidity and all complained of frequent sighing or gasping at rest, breathlessness with excitement or anxiety, breathlessness after trivial exertion, and inability to take a deep, satisfying breath.[11]

An emotional or "nervous origin" for constant or frequent sighing, not dependent on heart, lung, thyroid, or renal disease was noted more than 50 years ago.[12] Sighing, irregular respiration, breathlessness and overbreathing are often noted in emotionally unstable patients.[13,14] In normal young adults, none or one sigh (defined as 3 times tidal volume) may occur during 15 minutes with none to 3 sighs in normal older patients.[15] In contrast, patients with chronic anxiety and episodic dyspnea at rest or exertion, with normal or near normal pulmonary function tests, demonstrate large sighs at

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a rate of 4 to 25 per 15 minutes.[16] The frequency of sighing might be helpful in the diagnosis of an anxiety state when dyspnea is out of proportion to the values obtained with the usual cardiac and pulmonary function tests.[16]

Experimentally, psychogenic factors are known to alter the perception of dyspnea. Although the methodology may vary, a number of investigations demonstrate that stress increases respiratory rate, minute ventilatory volume, irregularity of breathing, alterations in tidal volume, and decreases alveolar and blood CO_2.[17] Naturally occurring stress and the suggestion of stressful situations can result in dyspnea. Some subjects develop dyspnea while other subjects, with seemingly identical emotional and physiologic change, do not develop dyspnea.[18] Persons with psychogenic respiratory disturbances overrate their degree of dyspnea during rest when compared to normal control subjects.[19]

Even in the presence of cardiopulmonary disease, the sensation of dyspnea or breathlessness may not be congruent with the disease process. There is a wide spectrum of performance, from those who appear to be disproportionately disabled to those whose performance exceeds expectations as predicted from their vital capacity. Among individuals 70 years of age with the subjective experience of dyspnea, 28% of the men and 43% of the women were noted to have dyspnea that was not related to disease, including cardiac failure, pulmonary disease and ischemic heart disease.[20]

Patients with chronic bronchitis may complain of breathlessness that cannot be adequately explained by the degree of airways obstruction. Their beliefs and attitudes may be better predictors of walking distance than ventilatory capacity or mood.[21] Among 31 patients with disproportionate breathlessness, all had the symptoms of an hysterical reaction, anxiety reaction, or depressive illness. They experienced hyperventilation attacks, difficulty getting air in, dyspnea at rest, and a poor relationship of breathlessness to exertion. Noisy inspiration and expiration, sighing with inspiratory laryngeal stridor, grossly irregular respirations, and the recent death of a spouse or relative were frequently noted in those patients with excessive dyspnea.[22]

Treatment

Treatment of these patients may be difficult and time consuming. The patients visit a physician because they perceive they have a physical problem and the problem must have a physical cause. When our evaluations fail to find an organic reason, they are often referred to a specialist for treatment. Since the patient is experiencing physical discomfort and not psychological discomfort, referral may be poorly received by some patients. The treatment might be better continued by the physician establishing the diagnosis since the patient perceives this physician as oriented toward the treatment of physical problems, and other specialists can be utilized as consultants. The same compassionate listener providing regular and frequent support is a major part of therapy.

Psychotherapy and drugs have been considered for the treatment of dyspnea associated with chronic obstructive lung disease.[23] However, the treatment of dyspnea in patients with normal lungs is rarely considered. Dihydrocodeine and promethazine may reduce the sensation of dyspnea in patients with chronic obstructive lung disease.[24,25] For disproportionately severe dyspnea in chronic bronchitis, the dyspnea in the depressive-illness group of patients may respond to a tricyclic antidepressant drug while the dyspnea in the anxiety-reaction group of patients may respond to diazepam.[22]

In patients with dyspnea due to chronic obstructive lung disease, psychotherapy provided by an experienced nurse without psychotherapeutic training reduced dyspnea in contrast to therapy provided by two experienced psychoanalysts.[26] In patients with panic attacks and dyspnea, treatment involves psychotherapy, psychotropic drugs, beta-adrenergic blocking drugs and behavior therapy.[4,9] Management of psychosomatic dyspnea must be individualized and will likely involve several modes of treatment.

A Psychiatrist's Viewpoint

Dr. Brashear's paper gives a comprehensive review of a symptom complex that is encountered very frequently in medical practice. The physician is confronted with a challenge once the symptom has been found to be inconsistent with existing disease or purely psychosomatic because, as is pointed out, it can occur in the spectrum of underlying psychiatric disorders.

As a part of a situational stress reaction, in a usually stable person, treatment would be supportive and brief, but it can appear as the presenting complaint in a complex personality disorder, hysteria, major depression or schizophrenia. The degree of urgency the patient expresses about the symptom, or appearing to be obsessively preoccupied with it, usually indicates a more serious underlying psychiatric disorder that should be specifically evaluated.

When psychosomatic dyspnea is a complication of existing compromised pulmonary function, the treating physician is in the best position to help the patient understand how the stress of illness can intensify the condition. If that reassurance, support and low dose anti-anxiety or anti-depressant medication are not successful, a more serious emotional problem probably exists.—**Ronald H. Hull, M.D., Indianapolis**

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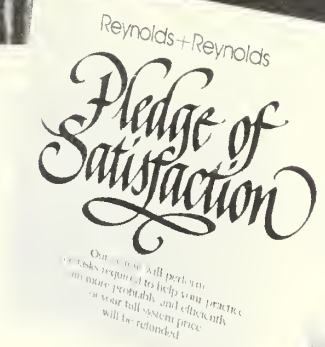
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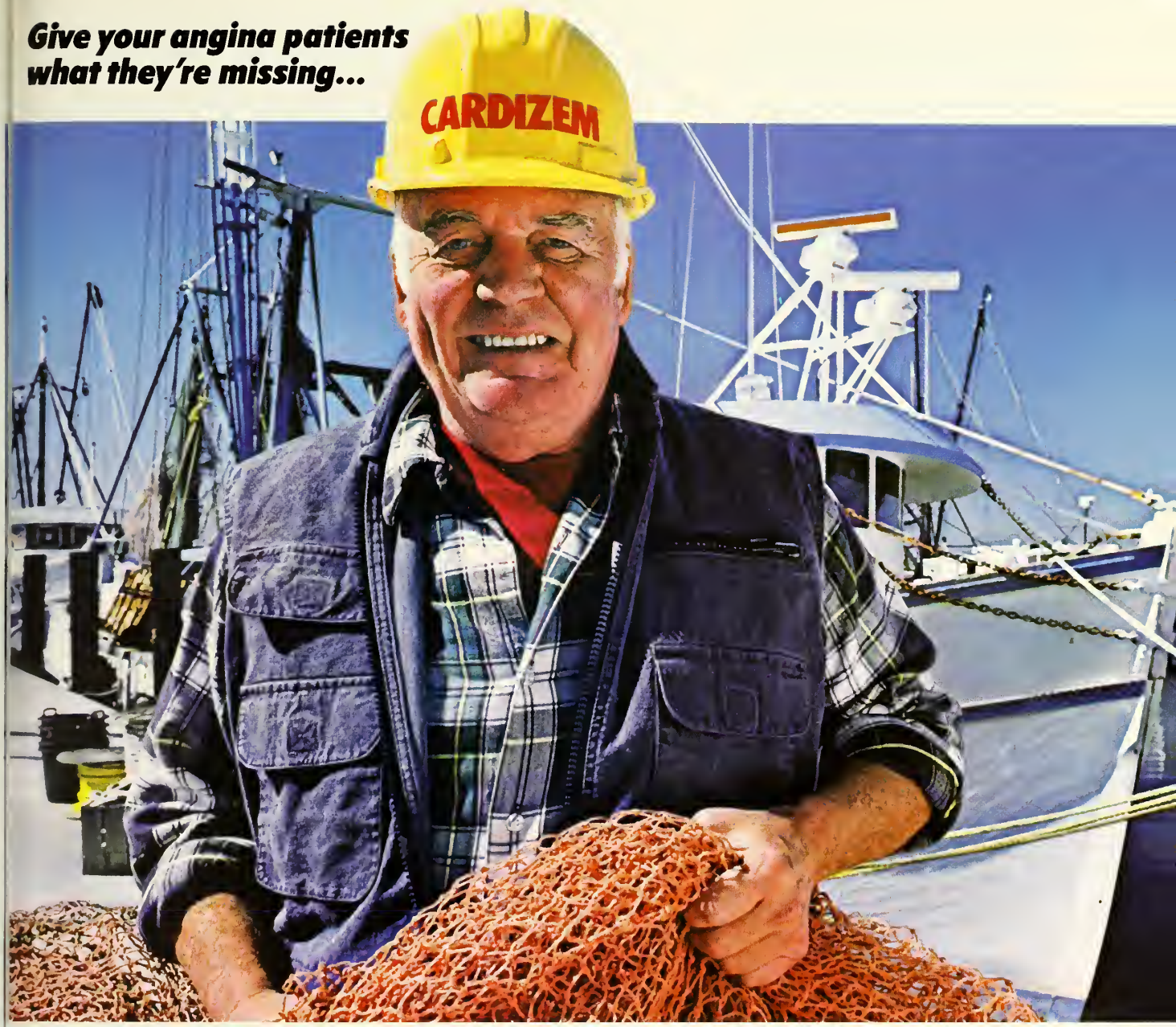
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CONTRAINDICATIONS
CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, and (3) patients with hypotension (less than 90 mm Hg systolic).

WARNINGS

1. **Cardiac Conduction.** CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (six of 1,243 patients for 0.48%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of diltiazem.
2. **Congestive Heart Failure.** Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt).
   Experience with the use of CARDIZEM alone or in combination with beta-blockers in patients with impaired ventricular function is very limited. Caution should be exercised when using the drug in such patients.
3. **Hypotension.** Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.
4. **Acute Hepatic Injury.** In rare instances, significant elevations in enzymes such as alkaline phosphatase, CPK, LDH, SGOT, SGPT, and other symptoms consistent with acute hepatic injury have been noted. These reactions have been reversible upon discontinuation of drug therapy. The relationship to CARDIZEM is uncertain in most cases, but probable in some. (See PRECAUTIONS.)

PRECAUTIONS
General. CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any new drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these changes were reversible with continued dosing.

Drug Interaction. Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS.)

Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers or digitalis is usually well tolerated. Available data are not sufficient, however, to predict the effects of concomitant treatment, particularly in patients with left ventricular dysfunction or cardiac conduction abnormalities. In healthy volunteers, diltiazem has been shown to increase serum digoxin levels up to 20%.

Carcinogenesis, Mutagenesis, Impairment of Fertility. A 24-month study in rats and a 21-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response in in vitro bacterial tests. No intrinsic effect on fertility was observed in rats.

Pregnancy. Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/posthatal studies, there was some reduction in early individual pup weights and survival rates. There was an increased incidence of stillbirths at doses of 20 times the human dose or greater.

There are no well-controlled studies in pregnant women, therefore, use CARDIZEM in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. Diltiazem is excreted in human milk. One report suggests that concentrations in breast milk may approximate serum levels. If use at CARDIZEM is deemed essential, an alternative method of infant feeding should be instituted.

Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS
Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded.

In domestic placebo-controlled trials, the incidence of adverse reactions reported during CARDIZEM therapy was not greater than that reported during placebo therapy.

The following represent occurrences observed in clinical studies which can be at least reasonably associated with the pharmacology of calcium influx inhibition. In many cases, the relationship to CARDIZEM has not been established. The most common occurrences as well as their frequency of presentation are: edema (2.4%), headache (2.1%), nausea (1.9%), dizziness (1.5%), rash (1.3%), asthenia (1.2%). In addition, the following events were reported infrequently (less than 1%):

Cardiovascular	Angina, arrhythmia, AV block (first degree), AV block (second or third degree — see conduction warning), bradycardia, congestive heart failure, flushing, hypotension, palpitations, syncope
Nervous System	Amnesia, gait abnormality, hallucinations, insomnia, nervousness, paresthesia, personality change, somnolence, tinnitus, tremor.
Gastrointestinal	Anorexia, constipation, diarrhea, dysgeusia, dyspepsia, mild elevations of alkaline phosphatase, SGOT, SGPT, and LDH (see hepatic warnings), vomiting, weight increase.
Dermatologic	Petechiae, pruritus, photosensitivity, urticaria
Other	Amblyopia, dyspnea, epistaxis, eye irritation, hyperglycemia, nasal congestion, nocturia, osteoarticular pain, polyuria, sexual difficulties

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: alopecia, gingival hyperplasia, erythema multiforme, and leukopenia. However, a definitive cause and effect between these events and CARDIZEM therapy is yet to be established.

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Penetrating Cardiac Injury: Can We Improve Survival?

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This paper, which represents the experience at Wishard Memorial Hospital from January 1980 through December 1984, was presented at the 1986 Indiana Chapter meeting of the American College of Surgeons; it received the Leonard Ensminger Award for the best paper in the trauma category.

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THE MORBIDITY AND mortality of patients sustaining penetrating cardiac trauma are greatly affected by prehospital, emergency department, and operating room management. The purpose of this study is to delineate the factors necessary for improvement in the outcome of patients with penetrating cardiac injuries.

The clinical course for each of 32 patients with cardiac injuries treated in a large urban trauma center during the last five years was analyzed with special attention to the type of weapon used, the time spent at the scene and in transport, Trauma Scores in the field and in the emergency department, amount of blood and crystalloid received, associated injuries, extent of cardiac injury, and operative procedures. Discriminant analysis was used to evaluate the contribution of each variable to survival.

The nature of the injury is the most significant determinant of survival. Fifty-six percent of patients with stab wounds survived (9 of 16), whereas only 16% of those with gunshot wounds survived (2 of 13) [$p < 0.02$]. The three shotgun wounds were single pellet injuries and all survived. Complex injuries involving multiple cardiac chambers had a higher mortality (83%) than isolated atrial (55%) or ventricular (47%) wounds. Field and emergency department Trauma Scores were highly correlated with survival; survivors had an average score of 10.9 in the field and 11.5 in the emergency department, compared to 2.5 and 1.6 for nonsurvivors [$p < 0.001$]. Operative mortality was 13% (2/15) in those who had "signs of life" in the emergency department.

Mortality due to penetrating cardiac trauma is acceptably low in patients with isolated chamber injuries and high Trauma Scores if definitive treatment can be initiated early in the patient's course. Minimizing prehospital intervention will result in earlier access to definitive care and may improve survival.[1]

Rapid and effective treatment of patients with penetrating cardiac injuries is essential for survival. Sixty to eighty percent of patients die before reaching the hospital. Minimizing prehospital intervention and prompt transport of patients may reduce mortality in patients with salvageable injuries.[1]

The purpose of this study is to analyze the impact of prehospital care and emergency room management on the outcome of a series of patients with penetrating cardiac injuries treated at a large urban trauma center during the last five years.

Patients and Methods

From January 1980 through December 1984, 32 patients with penetrating cardiac injury were treated at Wishard Memorial Hospital. Sixteen patients sustained stab wounds, 13 patients had gunshot wounds, and three had shotgun wounds. Despite emergent thoracotomy and vigorous resuscitation efforts, 14 patients died in the emergency department. Seventeen patients underwent operation; one patient with a shotgun pellet wound to the interventricular septum was merely observed. Patients with penetrating cardiac injuries comprised 8.0% (7/88) of all gunshot wounds to the chest seen during this five-year period and 6.7% (11/163) of all stab wounds to the chest. The patients' ages ranged from 8 to 61 years, with a mean of 27 years. As in most

large series of traumatic injuries, 81% of the victims were male and only 19% were female. Twenty-one of the patients were black, and 11 were white.

Complete pre-hospital records were available on 78% of the patients. Time from ambulance dispatch to arrival in the emergency department and time spent at the scene (field time) were tabulated. Condition of the patient at the scene and resuscitative efforts performed by emergency medical technicians were also noted. Eighteen of the 32 patients (56%) were brought into the emergency department in full cardio-respiratory arrest.

The Trauma Score (*Table 1*) was used to assess patient status and provide an index for prognosis. The Trauma Score is the sum of points assigned to respiratory rate, respiratory expansion, systolic blood pressure, capillary refill, and the neurologic variables of the Glasgow Coma Scale (eye opening, verbal response and motor response). Trauma Scores at the scene could be calculated for 94% of the patients, and Trauma Scores in the emergency department were available for all patients. In those patients in whom capillary refill was not recorded, an estimate based on blood pressure was used.[2]

A high index of suspicion is necessary to make the diagnosis of penetrating cardiac injury. Precordial location of the wound, elevated central venous pressure, and the triad of hypotension, muffled heart sounds, and distended neck veins were helpful in making the diagnosis. Chest x-rays were obtained in stable patients. Chest tubes, if needed, were placed after volume resuscitation was begun. Pericardiocentesis was performed only once.

An emergency left anterolateral thoracotomy was performed in all 18 patients arriving in cardiorespiratory arrest, and in an additional patient who deteriorated in the emergency department. Five of these patients were subsequently taken to the operating room. Eleven of the 12 remaining patients who went to the operating room were explored through a median sternotomy. The other patient, who had a wound in proximity to the right pulmonary hilum, underwent a right anterolateral thoracotomy which was extended across the sternum. All cardiac wounds were repaired using 3-0 polypropylene sutures reinforced with Teflon pledgets. Cardio-pulmonary bypass was not used.

For analysis of data, continuous variables were compared using Student's t-test. Discrete variables were compared with Fisher's exact test. Stepwise discriminant analysis was also performed. Results were considered significant at $p < 0.05$.

TABLE 1
Trauma Score

Respiratory Rate	10-24/min	4	
	24-35/min	3	
	36/min or greater	2	
	1-9/min	1	
	None	0	
Respiratory Expansion	Normal	1	
	Retractive	0	
Systolic Blood Pressure	90 mm Hg or greater	4	
	70-89 mm Hg	3	
	50-69 mm Hg	2	
	0-49 mm Hg	1	
	No Pulse	0	
Capillary Refill	Normal	2	
	Delayed	1	
	None	0	
GLASGOW COMA SCALE			
Eye Opening	Spontaneous	4	Total Glasgow Coma Scale Points
	To Voice	3	
	To Pain	2	
	None	1	14-15 = 5
			11-13 = 4
Verbal Response	Oriented	5	8-10 = 3
	Confused	4	5-7 = 2
	Inappropriate words	3	3-4 = 1
	Incomprehensible words	2	
	None	1	
Motor Response	Obeys Command	6	
	Localizes Pain	5	
	Withdraw (pain)	4	
	Flexion (pain)	3	
	Extension (pain)	2	
	None	1	
TOTAL TRAUMA SCORE			1-16

Results

Of the 32 patients in the series, 14 survived and 18 died, 14 of them in the emergency department. Distribution of age, sex, and race in both groups was comparable (*Table 2*).

Data on pre-hospital care are presented in *Table 3*. The mean time from radio dispatch of the ambulance to arrival of the patient in the emergency department was 26 minutes in survivors and 24 minutes in non-survivors (NS). Time spent by paramedics at the scene performing resuscitative measures was 12 minutes for survivors and 11 minutes for non-survivors (NS). This time was spent intubating moribund patients, initiating cardiopulmonary resuscitation, starting intravenous fluids, and administering oxygen and medications.

The duration of stay in the emergency department was highly variable. Surviving patients spent an average of 82 minutes in the emergency department. Non-survivors spent an average of 44 minutes (NS). These times, however, are skewed by a few stable patients who underwent prolonged evaluation in the emergency department.

Stab wounds and shotgun wounds were associated with a more favorable outcome than gunshot wounds (*Table 4*). Patients who sustained stab wounds had a 44% mortality (7/16). Gunshot wounds, however, were associated with an 85% mortality (11/13). All three shotgun wounds were single pellet rather than close range injuries and none was fatal. Data analysis (3x2 Chi-square) confirmed that the likelihood of survival was highly dependent upon the mechanism of injury ($p < 0.02$).

Field and emergency room Trauma Scores are listed in *Table 5*. Highly significant differences were obtained in comparing Trauma Scores in survivors and non-survivors. Survivors had an average field score of 10.9, and non-survivors had an average field score of 2.5. The emergency department scores for survivors averaged 11.5 and for non-survivors 1.6. There was one patient with a field score of 12 and an emergency department score of one who survived. No patient with a field score of one survived. *Figure 1* and *Figure 2* are graphic representations of the field and emergency department Trauma Scores, and the impact upon survival.

Emergency department thoracotomy was performed in 19 patients. Fourteen patients died in the emergency department; five of these patients were taken to the operating room and two survived. Thus, as might be anticipated, patients requiring emergency department thoracotomy had a poor prognosis (89% mortality).

The cardiac chambers injured are depicted in *Figure 3*. The percentage of penetrating wounds to each cardiac chamber is proportional to their anterior chest wall exposure. Thus, the

TABLE 2
Penetrating Cardiac Injury
1980-1984

VARIABLE	LIVING ($\bar{X} \pm SD$)	DEAD ($\bar{X} \pm SD$)	COMPARISON
Number	14	18	
Age	31.1 ± 13.8	23.9 ± 3.2	NS
Sex	11M 3F	16M 2F	NS
Race	5W 9B	7W 11B	NS

TABLE 3
Pre-Hospital Data

TIMES (in minutes)	LIVING ($\bar{X} \pm SD$)	DEAD ($\bar{X} \pm SD$)	COMPARISON
DISPATCH-ER	25.9 ± 9.5	24.3 ± 6.3	NS
IN FIELD	12.1 ± 6.2	11.1 ± 4.7	NS
IN ER	82.4 ± 107.5	59.3 ± 62.5	NS

TABLE 4
Penetrating Cardiac Injury

VARIABLE	LIVING	DEAD	COMPARISON
Stab Wound	9	7	NS
Gunshot	2	11 $p < .02$	$p < .03$
Shotgun	3	0	$p < .08$

TABLE 5
Trauma Scores

	LIVING ($\bar{X} \pm SD$)	DEAD ($\bar{X} \pm SD$)	COMPARISON
Field	10.9 ± 4.7	2.5 ± 3.1	$p < .001$
ER	11.9 ± 4.3	1.6 ± 1.5	$p < .001$

TABLE 6
Resuscitation

	LIVING ($\bar{X} \pm SD$)	DEAD ($\bar{X} \pm SD$)	COMPARISON
ER RL (Liters)	2.4 ± 1.5	2.4 ± 2.9	NS
ER_BLOOD (units)	0.2 ± 0.6	1.8 ± 3.4	$p = .07$
ER THORACOTOMY	2 yes 12 no	17 yes 1 no	$p < .001$

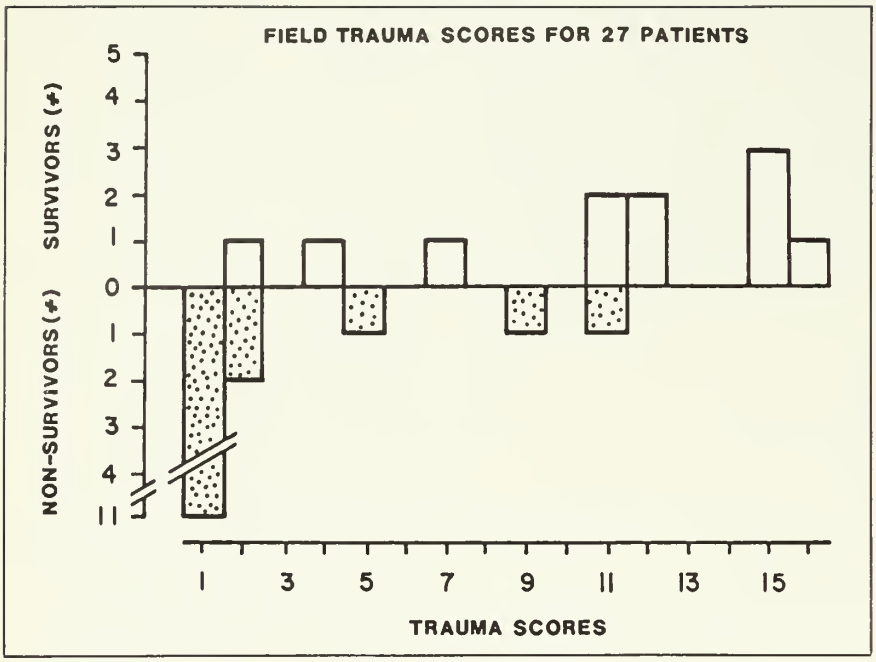


FIGURE 1

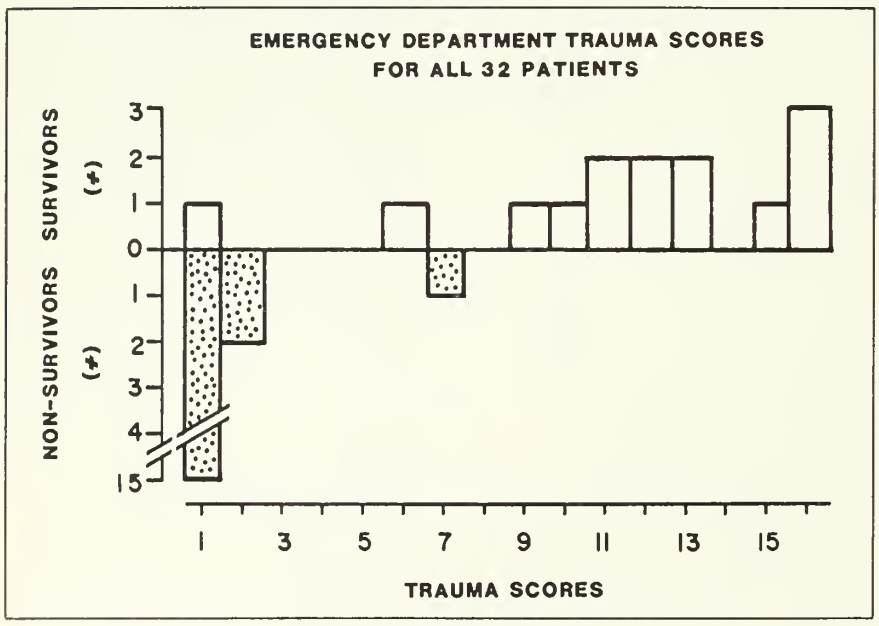


FIGURE 2

right ventricle was injured most often, followed by the left ventricle, and the right atrium/superior vena cava junction. An injury to the proximal left anterior descending coronary artery was lethal. Complex injuries involving multiple cardiac chambers had a higher mortality (83%) than isolated atrial (55%) or ventricular (47%) wounds.

Associated injuries were frequent (*Table 7*). Pulmonary parenchymal damage was the most common concurrent injury in patients with stab wounds. Four patients underwent exploratory laparotomy, and three had associated intra-abdominal injuries. Two patients sustained colon injuries, and both underwent combined laparotomy and median sternotomy. One of these patients developed a mediastinal abscess 15 days after admission, and suffered a cardio-respiratory arrest and anoxic encephalopathy. He also required drainage of an intra-abdominal abscess 37 days after admission.

Atelectasis and pneumonia were the most common postoperative complications, occurring in six patients. Other complications included prolonged ileus, pericarditis, rebleeding, and ventricular conduction defects. Two patients died in the early postoperative period, both declared brain dead after coagulopathy-related complications.

Four of the patients with penetrating cardiac injuries who reached the operating suite died, yielding an overall mortality of 23%. Two of these patients presented to the emergency department with Trauma Scores of one (no signs of life). If these patients are disregarded, overall operative mortality was 13%.

Discriminant analysis of the results was performed in an attempt to select a combination of variables that would predict survival or death (*Table 8*). Variables included in the analysis were age, Trauma Score in the emergency department and liters of crystalloid and units of blood given in the emergency department, complex injury, wounding agent, and emergency department thoracotomy. These variables were available for all 32 patients. Since this technique chooses variables which independently contribute to a discrimination between survivors and non-survivors, variables which are highly correlated with each other will not appear in the final results. As an example, Trauma Score and emergency department thoracotomy are highly correlated, therefore only one of the two variables will be selected as predictive.

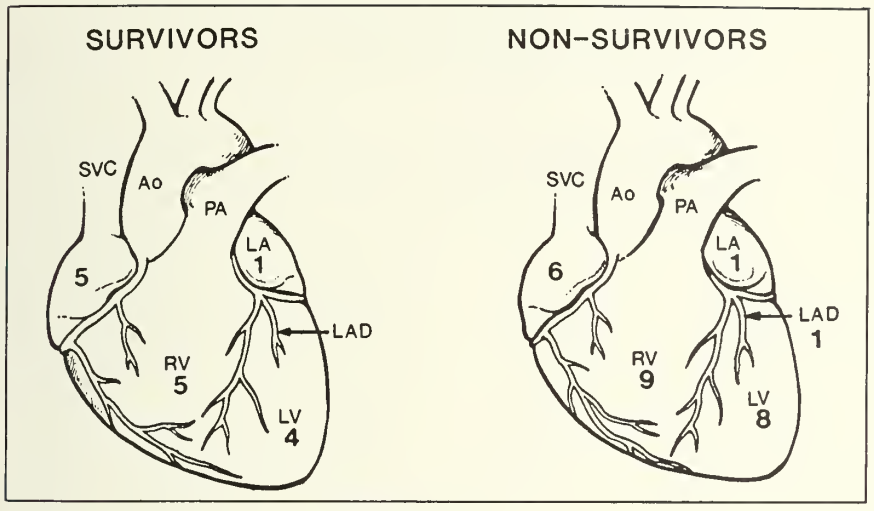


FIGURE 3

As seen in *Table 8*, the variables most predictive of outcome were Trauma Score in the emergency department and the wounding agent. The structure coefficient indicates the relative importance of the variables, Trauma Score being the better predictor. To use discriminant analysis as a predictor of survival, the value of each variable is multiplied by its function coefficient and a constant term (−.76) added. Values greater than 0.23 indicate a high likelihood of survival. This analysis accurately classified all but one patient in this series. Thus, higher Trauma Scores and knife wounds are predictive of improved survival rates.

The average hospital stay for 13 of the 14 survivors was 12 days (range 6-28), while one patient with anoxic encephalopathy and mediastinal abscess stayed 82 days.

Few data were available to evaluate long-term sequelae.

Discussion

The pre-hospital mortality in patients with penetrating cardiac injury is reported to be 60-80%.[3] Gunshot wounds usually present with exsanguinating hemorrhage and therefore have a poorer prognosis than patients with stab wounds, who generally present with cardiac tamponade.[4] Our series confirmed better survival in patients with stab wounds, 56%, as opposed to the 15% survival seen in patients with gunshot wounds.

Comparison of the results of our experience with other series is difficult. Most series rely on the blood pressure and descriptive words such as "moribund" or "unstable" to classify the condition of patients presenting to the emergency department. The Trauma Score has been demonstrated to be an accurate objective measure of survival in trauma patients,[5] and routine use of this numerical system would permit meaningful comparisons with other reported series. Our data confirm that the association between Trauma Score (physiologic condition), and mortality is highly significant ($p < 0.001$), both in the field and in the emergency department.

In this urban setting, most of our patients were transported over very short distances, requiring an average of only seven minutes for transportation. The average of 12 minutes spent at the scene by the emergency medical technicians may be excessive in this group of patients. Although intubation of moribund patients may be beneficial, overall better results may be achieved if emergency medical technicians "scoop and run" with patients. Placement of intravenous lines, administration of drugs, and securing pneumatic antishock trousers can be done during transport in the ambulance; and the most effective resuscitation in pene-

TABLE 7
Associated Injury

Survivors

SW	GSW
Pulmonary Artery	Liver, Stomach, Colon
Internal Mammary Artery	Lung
Diaphragm - 2	Stomach, Colon, Small Bowel
Lung - 4	Pancreas, Gallbladder
Extremity - 2	Omental Pellets
	Extremity - 2

Non-Survivors

SW	GSW
Pulmonary Hilum	Extremity
	Lung
	Esophagus, Hemiazygous, Inferior pulmonary vein
	Aorta
	Pulmonary hilum

trating cardiac injury can only be performed in the emergency department and operating room. Unfortunately, our series does not help to resolve this controversy, since scene and transport times were essentially identical in survivors and non-survivors. The issue can only be resolved by comparing the outcome in groups of patients in whom resuscitation at the scene was minimized and significantly shorter field times achieved.

Several authors have concluded that emergency room thoracotomy in patients without signs of life in the field or in transport is futile.[6,7] We performed emergency department thoracotomy on any patient with penetrating cardiac injury who entered the emergency department in cardiorespiratory arrest or who arrested in the emergency department. Of our patients without signs of life at the scene or in transport, none survived, although one patient with a Trauma Score of one in the emergency room did survive without neurologic sequelae.

The results of recent published series of patients with penetrating cardiac injuries who underwent emergency department thoracotomy are depicted in *Table 9*. Our mortality of 89% is comparable to that of other reports in similar patient groups. Eighty-four percent of the patients in our series presented with no vital signs or spontaneous movement (Trauma Score = one).

The operative mortality of 23% for the Wishard Memorial Hospital series is also comparable to that of other reported series (*Table 10*). If the two patients without signs of life on presentation to the emergency department are excluded, the mortality is 13%, similar to the Parkland[8] and San Antonio[9] series, with mortalities of 9.6% and 11%, respectively. The South African series, with 14.4% mortality,[10] describes a large number of patients, all of whom had to be transported long distances (up to 15 km.) over secondary roads, thereby selecting out those patients in the best physiologic condition for operation.

We recommend a left anterolateral thoracotomy instead of median sternotomy in cases of associated suspected gastrointestinal tract injury. Separation of the two incisions may result in a lower incidence of contamination and infection and provides adequate access to deal with almost any cardiac injury. A mediastinal abscess complicating the course of one patient in our series with a midline

TABLE 8
Disriminant Analysis

VARIABLE	STRUCTURE COEFFICIENT	FUNCTION COEFFICIENT	SIGNIFICANCE
Race 1W			
2B	−0.04	−1.56	$p<.001$
Trauma Score			
Field	0.33	0.24	$p<.001$
E.R.	0.50	0.23	$p<.001$
Stab Wound			
1 = yes			
2 = no	0.16	2.21	$p<.001$
Units of blood in ER	−0.09	−0.38	$p<.001$
Age	0.17	0.055	$p<.001$

TABLE 9
Penetrating Cardiac Injuries
ER Thoracotomy

STUDY	PATIENTS	% WITH NO VITAL SIGNS	% MORTALITY
Houston (1974)[16]	48	23	48
Boston (1978)[7]	38	unknown	76
New Orleans (1979)[13]	44	91	89
San Fran. (1980)[14]	63	54	72
So. Africa (1983)[10]	16	unknown	88
N.Y.-N.Y.M.C. (1983)[15]	91	58	73
Baltimore (1984)[4]	37	35	43
Indianapolis - WMH	19	84	89

TABLE 10
Penetrating Cardiac Injury
Mortality

STUDY	DATES	PATIENTS	% MORTALITY
Wishard Memorial Hospital	1980-1984	17	23
Parkland[8]	1976-1981	156	9.6
Louisville[17]	1974-1977	42	13.
So. Africa[10]	1978-1980	104	14.4
San Antonio[9]	1968-1978	100	11.
Birmingham[18]	1970-1980	46	23.

laparotomy for a colon injury and a simultaneous median sternotomy was associated with significant morbidity and prolonged hospitalization.

The importance of late follow-up in patients with penetrating cardiac injuries has also been emphasized in the literature. A 20-25% incidence of residual or delayed cardiac sequelae has been noted.[11,12] As a minimum, we recommend a follow-up echocardiogram be obtained; if abnormal, cardiac catheterization should be performed.

Discriminant analysis selected emergency department Trauma Score and the type of injury as the independent variables important in determining survival. Field Trauma Scores and the need for emergency room thoracotomy were highly correlated with these variables, but also demonstrated independent statistical significance. Other variables tested—including age, sex, race, scene and transport times, fluid and blood given in the emergency department, time spent in the emergency department, and the presence or absence of complex wounds—did not demonstrate significance or help discriminate between survivors and non-survivors.

A patient with a high Trauma Score who presents with penetrating cardiac injury due to a stab wound has a significant survival advantage over a patient who presents with a gunshot wound and a low Trauma Score. Therefore, survival is most dependent upon the nature of the injury. Survival may be improved if resuscitative measures at the scene are minimized.

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Survival after Left Heart Assist

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HENRY F. OLIVIER, JR., M.D.
Indianapolis

PROFOUND LEFT AND right ventricular failure following cardiac surgical procedures has decreased considerably in the past several years. Improved surgical techniques, better intraoperative myocardial preservation, and modern methods of afterload reduction have all contributed to this fact. However, there is still a small percentage of patients who remain in cardiogenic shock following heart surgery and cannot be weaned from standard cardiopulmonary bypass.

Reports indicate that this impaired ventricular function, in some instances, may only be temporary. A degree of significant ischemic injury occurs which may only "stun" the heart, thereby interfering with normal biochemical processes and ultrastructure, and consequently depressing function.[1] Causes of this dysfunction may be perioperative ischemia, inadequate intraoperative myocardial protection, incomplete revascularization, air embolization, or reperfusion injury. If short-term support can be provided, the myocardial injury may be reversible, and the patient may be saved.

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Case Report

On Dec. 17, 1985, a 57-year-old man with COPD and unstable angina was admitted to Community Hospital of Indianapolis. Standard treatment with narcotic analgesia, topical and intravenous nitrates, and Beta blockade failed to provide relief of symptoms. On 12/18/85, the patient underwent left ventricular and coronary angiography. He was found to have critical triple vessel coronary artery disease. While in the cath lab holding area following the procedure, he suffered a cardiac arrest with loss of consciousness and complete heart block. Attempts to resuscitate him using standard techniques of mechanical ventilation, external cardiac massage, transvenous pacing, cardiotropic agents, and intraaortic balloon (IAB) counterpulsation failed to maintain a mean arterial BP of 50. The left common femoral artery and vein were cannulated, and he was placed on partial cardiopulmonary bypass while still in the catheterization laboratory. Two hours of cardiopulmonary resuscitation was provided from the time of arrest until he reached the OR.

At surgery a four-vessel coronary artery bypass was performed. The patient had a large, poorly contracting heart and an inferobasilar scar from a previous inferior MI. Attempts to wean him from cardiopulmonary bypass using optimization of preload and afterload, therapeutic infusions of Dopamine and Adrenalin, as well as IAB counterpulsation were unsuccessful. A left heart assist (LHA) device was connected to cannulas in the left atrium and aorta utilizing the Biomedicus centrifugal pump (*Figure*).

In the postoperative recovery room the patient was arousable and neurologically intact. With an LHA flow of 4 L/min the patient's cardiac index (CI) was maintained at greater than 2 L/min/m^2. His course was complicated by bleeding, acute renal failure, and acute respiratory distress syndrome (ARDS). Twenty-four hours later he was weaned from the LHA and returned to the OR for cannula removal and proper sternotomy closure. He was still maintained with Dopamine and the IAB. The latter was eventually removed on the fourth postoperative day. Further complications included Serratia marcescens pneumonia, a flail chest, ARDS requiring a tracheostomy, and atrial fibrillation requiring cardioversion. He did recover fully and was released from the hospital six weeks from the time of cardiac arrest.

History

The use of temporary circulatory support in humans began with the first clinical application of cardiopulmonary bypass by John Gibbon in 1953.[2] In the early 1960s Dennis,[3] Stuckey,[4] and others began to employ LHA for cardiogenic shock. Left ventricular bypass was first used successfully by Spencer in 1964[5] and DeBakey[6] in 1966 for postoperative low cardiac output. In the past 10 years there has been an evolution of ventricular assist devices (VAD) to maintain support for the injured or "stunned" heart to allow recovery. This is especially necessary in a situation of low cardiac output (CO) syndrome following technically successful cardiac surgery.

Discussion

The rationale for using a VAD is that a potentially reversible perioperative myocardial injury has occurred. In the critical period following surgery there are two considerations, the pumping ability of the heart and the maintenance of vital organ system function. VAD are important to both. Although

the role of VAD has expanded to include patients with ventricular failure due to cardiogenic shock following MI,[7,8] and patients awaiting cardiac transplantation,[9,10] postoperative cardiogenic shock remains the predominant indication for their use.[11]

Criteria have been developed and modeled after Norman[12] for cardiogenic shock patients. Upon weaning from conventional cardiopulmonary bypass (CPBP) one attempts to optimize preload by maintaining right atrial (RA) or left atrial (LA) pressures greater than 20 mmhg. Afterload reduction is provided by IAB support and peripheral vasodilators. Cardiac stimulants such as Dopamine, Isuprel, or Adrenalin are used to maximize CO. LHA is indicated if CI remains less than 2 L/min/m^2, systolic blood pressure is below 90, systemic vascular resistance (SVR) is greater than 2100 dynes-sec-cm^2, RAP and LAP are over 20, and urine output is less than 20 cc/hr.

Types of VAD

There are three types of commonly used non-pulsatile assist devices:

1. Medtronic centrifugal pump (MedCP) (Medtronic, Inc., Minneapolis). This is a non-pulsatile blood pump that propels blood with a rotating impellar. It has only one moving part, a rotor that is magnetically coupled to an external drive unit.

2. Bio pump (Biomedicus, Inc., Minneapolis). This is a vortex pump with valveless rotator cones made from nonthrombogenic acrylics. This imparts a centrifugal motion to the blood. The flow path is designed to eliminate turbulence and cavitation of air. This, in turn, reduces damage to the blood elements.

3. Standard extracorporeal membrane oxygenator (EMCO). This utilizes a membrane oxygenator and an arterio-venous circuit driven by a roller pump. Because of the need for heparinization, bleeding is a problem with this method.

There are two types of pulsatile

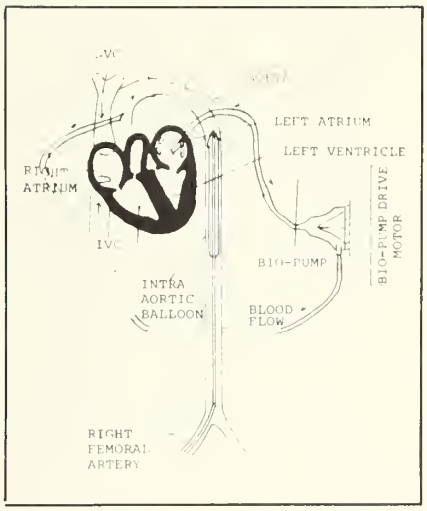


FIGURE: Blood is collected in the left atrium, circulated through the vortex pump and then is pumped to the aorta, effectively bypassing the patient's left ventricle, thereby giving it a chance to heal.

VAD:

1. Pierce-Donachy (Thoratec Corp., Berkley, CA.) This is a paracorporeal pneumatic sac type device constructed of a polycarbonate housing containing a flexible seam-free segmental polyurethane sac. The VAD utilizes Bjork-Shiley tilting disc inlet and outlet valves.

2. Jarvik Artificial Heart. This is an implantable pump with external pneumatic drive. Emboli have been a problem.

Pulsatile assist devices are hampered by high cost and the sophistication required for effective operation. The less complicated non-pulsatile systems are less expensive to acquire and maintain. They are simple to insert and easy to manage. In most instances with the non-pulsatile devices, pulsatile flow is provided by the IAB and to some extent by the natural output of the heart.

Summary

Current reports indicate that more than 200 patients have been treated with short-term VAD.[1] They suggest that the occurrence of perioperative MI is an important negative influence on survival while preoperative ventricular function is not.[13] Although respiratory failure is often reversible, the development of severe renal failure almost always precludes survival.[7,11,14-17] Most patients of this type die of sepsis and multiple organ failure. Although fewer than 20% of postoperative patients requiring VAD survive, studies by Pennington, *et al.* indicate that long-term quality of life is excellent. Beneficial results of these VAD have been well documented.[18]

The case report herein is an example of the use of an innovative device and technique in a community hospital setting. It allowed the survival of a patient who would otherwise have died. He was able to overcome all the complications of profound cardiogenic shock, recover, and go on to lead a satisfying, useful existence.

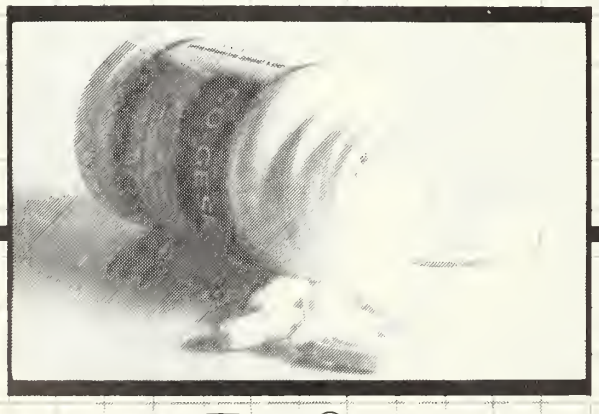
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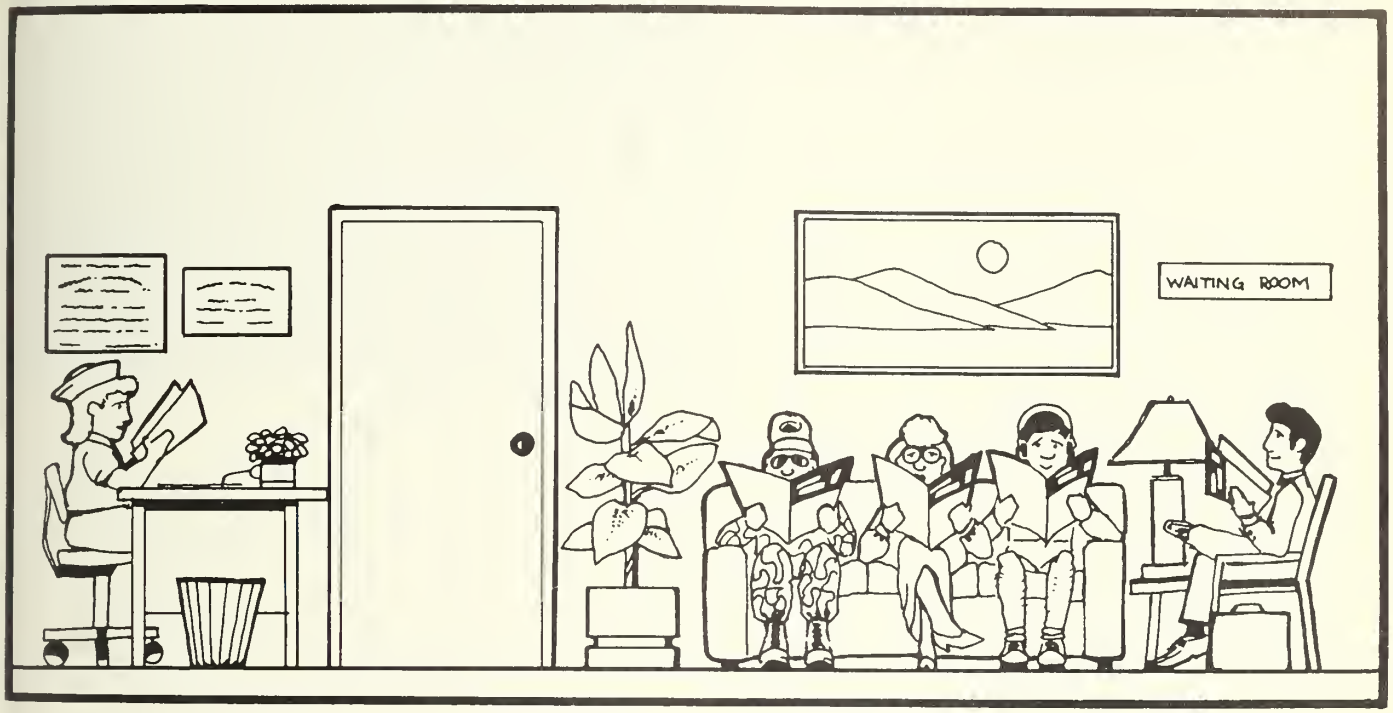
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Medicine's Lighter Moments

TED L. GRISELL, M.D.
Indianapolis

ONE OF THE interesting stories emanating from the old Indianapolis City Hospital concerned an elderly man who was admitted for emergency surgery because of a perforated peptic ulcer.

The day he was admitted, things were a bit hectic; accident cases were filling the emergency room, and everyone was in a hustle and a bustle. Before being taken to surgery, the patient's belongings were heaped in a pile and bagged and tagged. They were returned to him shortly after he recuperated from his anesthesia.

In the process, the man's brand-new dentures, which his family dentist had provided him less than a week before, had disappeared.

The economics of the City Hospital at that time were considerably more acute than possibly at present. So, as the resident in charge of the patient's surgery, I asked the hospital's dental intern to make an impression and then see if replacement dentures could be made through the dental school facilities—perhaps at a reduced cost or even free of charge.

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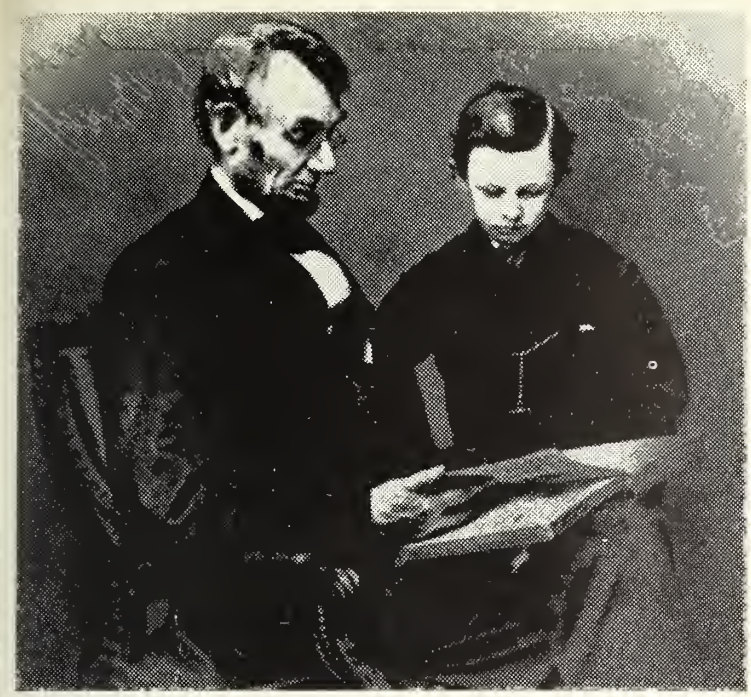
THE TEETH

Since the family dentist happened to be a personal friend, I also mentioned to him that we had misplaced the man's dentures and that, within a day or two, he would be able to eat and would need his teeth. The family dentist was saddened and concerned about his patient's plight.

Two days later, the dental resident appeared with a new set of teeth that he had made for the gentleman. As he was giving them to the patient to try, the family dentist arrived. He, too, had brought a new set of dentures, which he had made from the impressions he had taken some weeks earlier.

The patient laughed and slipped his hands behind his head as he lay back in laughter. As he did so, he felt something hard in his pillow case. He reached inside and discovered that he had stashed his first set of teeth in the lining of the pillow case.

As a result, the gentleman probably was the only patient discharged from the old Indianapolis City Hospital with a different set of teeth for breakfast, lunch and dinner.



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Hospital Medical Staff Bylaws: An Indiana Model

ROBERT W. HOLDEN, M.D.
GEORGE C. MANNING, M.D.
DEAN L. STRYCKER, M.D.
RONALD L. DYER, J.D.
JONATHAN P. GENTILE, M.D.
JOE C. CHRISTIAN, Ph.D.

IN 1985, THE Hospital Medical Staff Section (HMSS) of the Indiana State Medical Association (ISMA) held its organizational meeting and decided its early major emphasis should be the development of a set of model medical staff bylaws. It was the intent of the group that these bylaws should be applicable for most medical staffs practicing in Indiana hospitals.

Throughout the remainder of 1985 and early 1986, the authors as representatives of the Indiana HMSS deliberated over a proposed set of bylaws. Upon completion of this model set of bylaws, they were submitted to the chief of staff and administrator for each of the 127 hospitals in Indiana. Both administration and the medical staff were asked for comments, and joint meetings were held. Subsequently, the model bylaws were amended and then submitted to the Indiana State Medical Association Board of Trustees for their review. The model bylaws were also reviewed by the Indiana Hospital Association, which in turn submitted recommended changes in the model bylaws with subsequent amendment.

Correspondence and reprints: Robert W. Holden, M.D., Dept. of Radiology, Wishard Memorial Hospital, 1001 W. 10th St., Indianapolis, Ind. 46202.

The HMSS held its second annual meeting on September 7, 1986, at which time the group reviewed, amended and approved the model bylaws. These bylaws were presented to and approved by the ISMA House of Delegates on November 2, 1986.

The medical staff bylaws, upon approval by the hospital medical staff and the governing body, establish the rights and responsibilities of each hospital staff member to the medical staff and the relationship of the organized medical staff to the hospital governing board. This mutual agreement is also required in any changes of the medical staff bylaws, i.e., neither the medical staff nor the governing body may unilaterally amend the bylaws.

Bylaws Create a System of Mutual Rights and Responsibilities Among Members of the Staff as Well as Between the Medical Staff and the Hospital . . .

This set of rules and regulations provides the legal framework that describes the organization of both administrative and clinical health care delivery within the hospital. While national monographs have been prepared for review, it is unusual to have a model bylaws presentation because of the uniqueness of state law and the individual hospital medical staff. This approved bylaws model is consistent with Indiana law but will require modification for each individual hospital.

Specifically, in Indiana the regulatory authority for hospital health care delivery is the Indiana State Board of Health. IND. CODE 16-10-1-6.5 states the governing board of the hospital is the supreme authority in the hospital and, with the advice and recommendations of the medical staff, is responsible for the appointment of the members of the medical staff and the assignment of privileges consistent with their individual qualifications. The medical staff of a hospital must be an organized group, and is responsible to the governing board for the clinical and scientific work of the hospital and for providing advice regarding professional matters and policies.

IND. CODE 16-12.1-3-1 states boards of county hospitals are responsible for the appointment and delineation of privileges of the medical staff, with the advice and recommendations of the medical staff. (410 IAC 15) states the medical staff of a hospital composed of two or more physicians is an organized group that is responsible to the governing board for the clinical and scientific work of the hospital. With the approval of the board, it must adopt bylaws that set forth qualifications for staff membership and provide a mechanism to carry out medical staff functions (410 IAC 15-1-7). Only licensed practitioners who are members of the medical staff may admit patients (410 IAC 15-1-10).

In addition to the above state law, the legal status of the medical staff has been determined by custom and usage, longstanding traditional relationships,

and accreditation standards of the Joint Commission of Hospitals. In Indiana, the law states clearly the supreme authority of the hospital is the governing board. It is also obvious that the governing board of the hospital cannot practice medicine and must entrust its hospital medical staff with the responsibility of providing quality care.

This entrusting relationship becomes a difficult legal question. There are those who argue that the medical staff has no self-governing authority in the manner usually ascribed to a legal entity and functions under authority delegated by the governing body. In contrast, today most physicians believe the governing body cannot delegate or supervise those functions that it cannot itself exercise. Therefore, this second line of reasoning supports the premise that the medical staff is a self-governing entity accountable to the hospital governing board.

During its 1986 annual meeting, the AMA House of Delegates adopted Report AA of the Board of Trustees, which highlights: (1) the medical staff should be recognized as professionally independent in exercising medical judgment, although accountable to the hospital governing body for overall performance; (2) the medical staff's authority arises by contract from bylaws adopted by the medical staff and approved by the governing body; (3) the governing body authorizes rather than delegates professional functions to the medical staff; and (4) the medical staff should be recognized as self-governing.

Increasingly, this relationship is being considered to be a contractual agreement. In a recent decision, *Terre Haute Regional Hospital, Inc. v. El-Issa*, 470 N.E.2d 1371 (Ind.App. 1st Dist., 1984), the Court stated that under Indiana law there must exist mutual obligations under an agreement before it will be treated as a valid enforceable contract. The Court further ruled that the medical staff bylaws, once approved by the Board, constitute a contract between a member of the medical staff and the hospital.

As stated previously, the unquestioned charge of all medical staffs is the responsibility for delivery of quality health care. The medical staff that performs this charge in behalf of the hospital and fulfills hospital responsibilities imposed by licensure and accreditation is self-governing. The Joint Commission on Accreditation of Hospitals (JCAH) Standards require "a single organized medical staff that has the overall responsibility for the quality of all medical care provided to patients and for the ethical conduct and professional practices of its members, as well as for accounting thereof to the governing body."

Medical staff bylaws enable the organization of the medical staff and thus help the medical staff to fulfill its responsibility to provide quality medical care. The Indiana Model Medical Staff Bylaws define the medical staff's organizational structure and outline the purposes and functions that the medical staff agrees to perform. These bylaws include provisions for self-governance, credentialing, due process, corrective action, and quality assurance review and evaluation.

Socioeconomic changes in the past few years are placing health care increasingly into the competitive marketplace. Thus, the practicing physician is required to pay more attention to the administrative aspects of medicine both in the office and hospital.

As the hospital undergoes change, the medical staff member must be concerned not only with the actual delivery of care but also with the administrative aspects of medicine that underlie and make the practice of medicine possible. For example, several localities in the nation are facing intense practice competition with restrictive credentialing of medical staff. Medical staff bylaws should be clear about criteria for appointment and privileging. Competition brings about adversaries and thus legal actions. Medical staff bylaws must be precise in due process and corrective action procedural policy. Prospective pricing systems are affecting some hospital staffs' credentialing and quality assurance. The bylaws must maintain professional independence free from lay interference that may be influenced by fiscal considerations, as for example, potential conflicts with the legitimate interests of shareholders in investor-owned hospitals.

The physician's foremost obligation is providing quality care to his patient—it is the basis of public trust in physicians. Quality care is difficult to measure and when measurements are attempted, conflict usually results. In the hospital, the physician's address of conflict is found in the medical staff bylaws. This document can create a system of mutual rights and responsibilities among members of the staff as well as between the medical staff and the hospital. Do your hospital's medical staff bylaws create an environment in which the professional can provide quality care to his patient? If you have any doubt, the bylaws committee of your medical staff should be asked to compare the existing bylaws against those of the Indiana Model Medical Staff Bylaws.

In summary, hospital medical staff bylaws are extremely important in today's health care environment. The written communication of intent by the medical staff and acceptance by the governing body create documented rights and responsibilities. Bylaws should be desired by both the medical staff and the governing body since adversarial posturing and ill-defined rules and regulations promote conflict and lawsuits. Effective communication and precise rules and regulations are the only answer for control of the increasing stress produced by peer review, prospective pricing systems, competition, cost efficacy, quality assurance, and restrictive credentialing.

'AIDS Doesn't Come and Get You—You Go and Get AIDS'

State Board of Health Planning Major, Statewide AIDS Conference

Stopping the spread of AIDS will require changing the general public's attitudes about their own sexual activities, not just education and counseling aimed at specific high-risk groups.

That's the message state and federal health officials presented recently to a group of AIDS community action program leaders from around Indiana.

"Something I've been telling people in my presentation is that when you have sex with someone, you're also having sex with everyone they've ever had sex with," explained Deborah Taylor, AIDS Coordinator for the Indiana State Board of Health.

Unless you can verify that the person with whom you're having sexual relations has not been infected with the virus responsible for acquired immune deficiency syndrome, all sexual relations should be considered at risk, she noted, adding, "AIDS doesn't come and get you, you go and get AIDS."

The disease, which has no cure and is invariably fatal, "is almost everywhere we go (in Indiana)," Taylor noted. "No matter where we go, we'll find a relative or a friend or someone with AIDS." On a recent speaking trip to one of Indiana's smallest towns, Taylor was approached by the family of an AIDS victim.

"They were all in tears because they had a daughter who was dying of AIDS," she said.

On the federal level, a spokesman for the Centers for Disease Control in Atlanta says more emphasis must be made on preventing all sexually transmitted diseases—not just AIDS.

"AIDS basically is a sexually transmitted disease," explained Fred Martich of CDC. "The virus is the enemy. AIDS is just the end result, so we have to stop transmission (of the virus)."

Martich, who was in Indiana in November as part of an extensive visit throughout the Midwest to meet with local health officials, said once a person becomes infected with the AIDS virus, other venereal diseases such as chlamydia and syphilis become even more dangerous. That's because the infected person's immune system is weakening, leaving him more susceptible to infection and complications.

There also is evidence, Martich reported, that frequent exposure to other diseases may hasten the onset of AIDS once a person is carrying the AIDS virus.

As part of thir effort to combat the disease here, Indiana State Board of Health officials are planning a major, statewide AIDS conference—titled "AIDS In The Heartland"—for February 6-7, 1987. The seminar, which is expected to attract nearly 2,000 health professionals and other interested parties to Indianapolis, will feature presentations from some of the nation's top experts in AIDS.

AIDS Education Program Wins Recognition

The Indiana State Board of Health's campaign against AIDS has been recognized by state officials from outside Indiana as one of the most innovative state government programs in the country.

The ISBH's Statewide AIDS Education Coordination program was selected by the Council of State Governments from more than 500 applicants to be one of only eight programs included in its 1987 Innovations series. The series examines programs which use new and innovative approaches to solving traditional problems facing state governments.

"We have made the fight against AIDS one of our highest priorities at the Indiana State Board of Health," explained Dr. Woodrow A. Myers, Jr., State Health Commissioner.

"This award shows that Indiana is doing the kind of job that needs to be done. We're proud that our efforts will be used as a role model that other states can use to develop their own programs," Dr. Myers added.

A yearlong case study will be conducted on the ISBH program and the results will be distributed to state officials nationwide so they may benefit from Indiana's experience in this area.

The ISBH AIDS program was praised for its efforts in assisting local community efforts against the deadly disease. In the program's first six months, AIDS education programs were presented in more than 75 percent of Indiana's 92 counties.

The anti-AIDS program also was the only public health program included among the eight selected.

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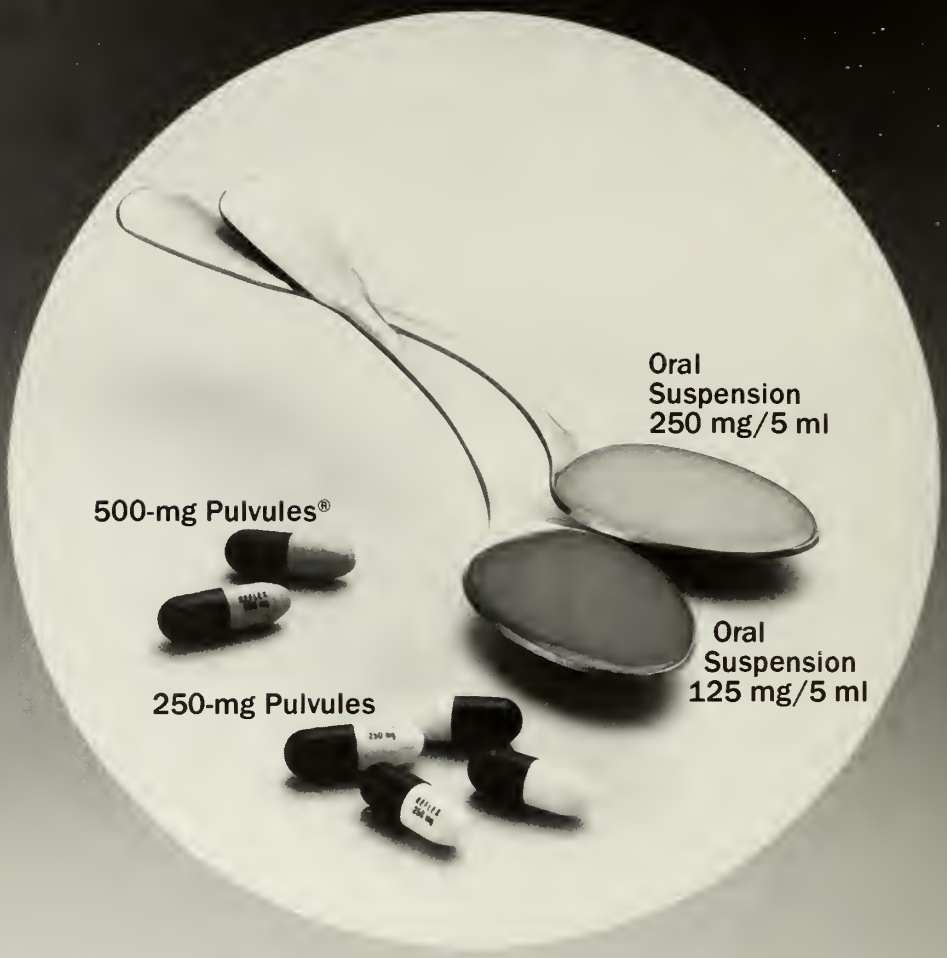
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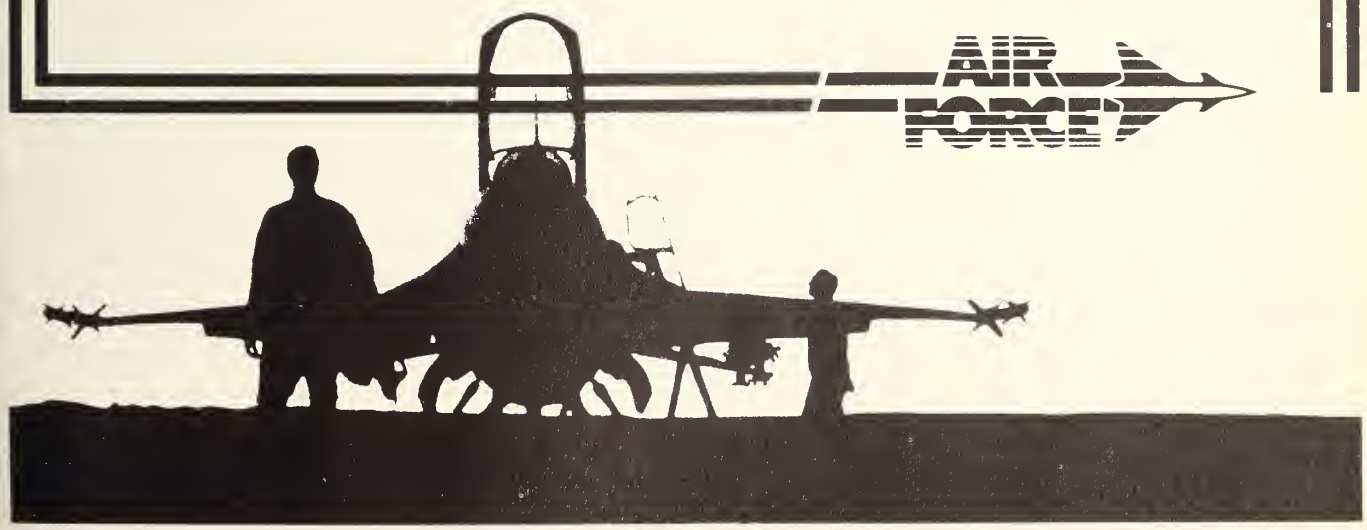
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AIR FORCE



1986 CONVENTION REPORT

Photos by
Ed Lacey, Jr.
Indianapolis



Members of the Capital City Council, Girl Scouts of the United States, post the colors during opening ceremonies of the House of Delegates.



Dr. Fred W. Dahling, speaker of the House, addresses delegates during the 137th annual convention.



Mrs. Dolores Herman of the ISMA staff greets Dr. Dwight W. Schuster of Indianapolis at the Registration Desk.



Dr. Paul Siebenmorgen delivers the president's address during the opening session of the House.



Mrs. Debbie Stroessner, executive director of the Vanderburgh County Medical Society, discusses the convention itinerary with Dr. Thomas H. Gootee of Jasper.



Marion County physicians (from left) Dr. James E. Cassady, Dr. I. E. Michael and Dr. Douglas H. White chat while awaiting the start of the Internal Medicine meeting.



Dr. Siebenmorgen answers questions from WRTV-Channel 6 reporter Angela Cain following a news conference on ISMA-sponsored tobacco resolutions.



Dr. John J. Coury, AMA president, addresses ISMA delegates during the first session of the House.



Dr. E. Larry Knight, an Elkhart County delegate, checks in with Mr. Howard Grindstaff of the ISMA field staff prior to being admitted to the House.



Dr. Donna J. Meade and Dr. Robert W. Mouser of Marion County listen to Reference Committee reports during the final House session. Dr. Meade is ISMA's first woman trustee.



Dr. Donald J. Kerner of Indianapolis, chairman of Reference Committee 3 (Legislation) listens to the testimony of Dr. John W. Beeler (standing, right).



Newly installed members of the ISMA Fifty Year Club. (A complete listing appeared in the October 1986 issue.)



Mrs. Sylvia Scheeringa, Auxiliary health projects chairman, discusses this Auxiliary exhibit with an interested visitor.



Resident physicians Dr. Dave Black (left) and Dr. Michael Williams exchange ideas during a reception following the ISMA-RMS sponsored practice opportunity session.



Two computer products exhibitors discuss their wares while awaiting physician traffic. Some 29 commercial exhibitors participated in this year's convention.



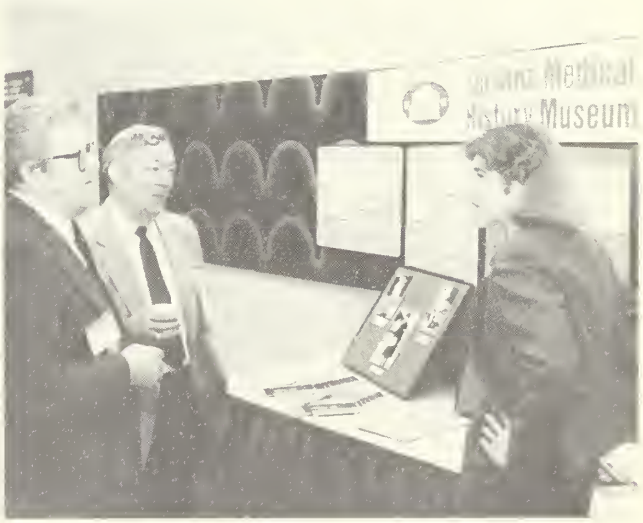
Besides pharmaceutical companies, exhibitors included insurance companies, treatment centers, computer and financial firms, medical laboratories, employee and auto leasing firms, and the Armed Forces.



Dr. Hamlin Lindsay of Washington, Ind., stops at the Eli Lilly and Company exhibit to discuss the company's various pharmaceutical products.



Dr. Charles A. Bonsett of Indianapolis (right) and Mr. John Whitaker chat in front of Indiana University's CME exhibit. Mr. Whitaker is the Graphic Arts producer-director for the Medical Educational Resources Program (MERP).



Miss Kathy McDonnell of the Indiana Medical History Museum answers the questions of Dr. T. Neal Petry of Delphi and Dr. Richard B. Schnute of Indianapolis.



Dr. and Mrs. Siebenmorgen greet Dr. John A. Knote (left center) and Dr. Woodrow A. Myers during the President's Reception.



Astronaut Donald E. Williams, a U.S. Navy captain, autographs photos for Dr. John Hinton of Liberty and his family.



Captain Williams, NASA astronaut and AIDME guest speaker, is flanked by David Khalouf, 14 (left) and Christian Keen, 10, during a luncheon reception sponsored by the Auxiliary.



Dr. Richard Reedy of Yorktown (center) speaks with the Democrat and Republican candidates for Indiana Secretary of State during the IMPAC luncheon.



Evan Bayh and his wife, Susan, are greeted by Dr. Siebenmorgen following the IMPAC luncheon. Mr. Bayh was successful in his bid for the office of Indiana Secretary of State.



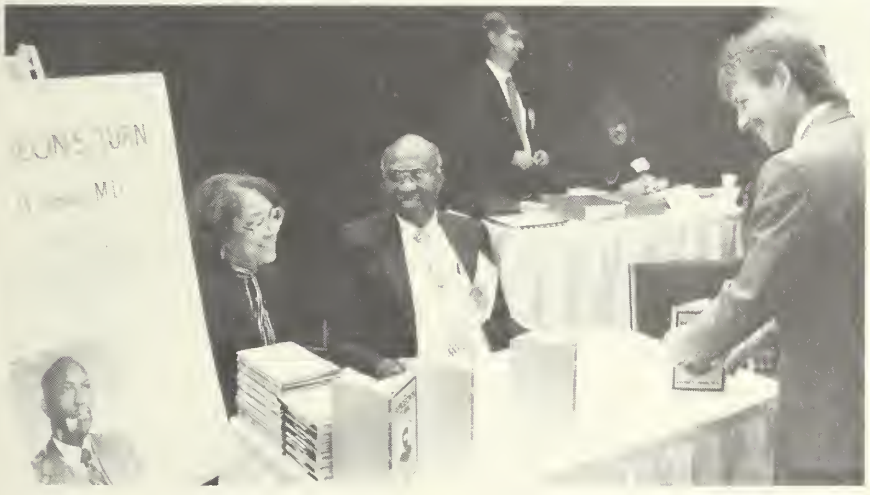
Kevin Walker (left), director of the AMA's Dept. of State and County Relations, and Richard R. King, ISMA executive director, chat with Rob Bowen, Republican candidate for Indiana Secretary of State.



Mrs. Alfrieda Mackel, ISMA Auxiliary president, gets a round of applause after being presented a bouquet by Dr. Siebenmorgen.



Dr. Alvin J. Haley (right), a member of the INDIANA MEDICINE editorial board, presents an ISMA Certificate of Merit to Dr. Mark W. Bradley of Indianapolis, one of three winners in the annual medical essay contest sponsored by the Resident Medical Society and INDIANA MEDICINE.



Mr. Harry Hoyle of Muncie (right) examines a copy of "The Surgeon's Turn," a new book written by Dr. George H. Rawls of Indianapolis (center). Dr. Rawls was joined by his wife at an autograph session.



Dr. Khalouf, ISMA president, and Dr. John D. MacDougall, president-elect.



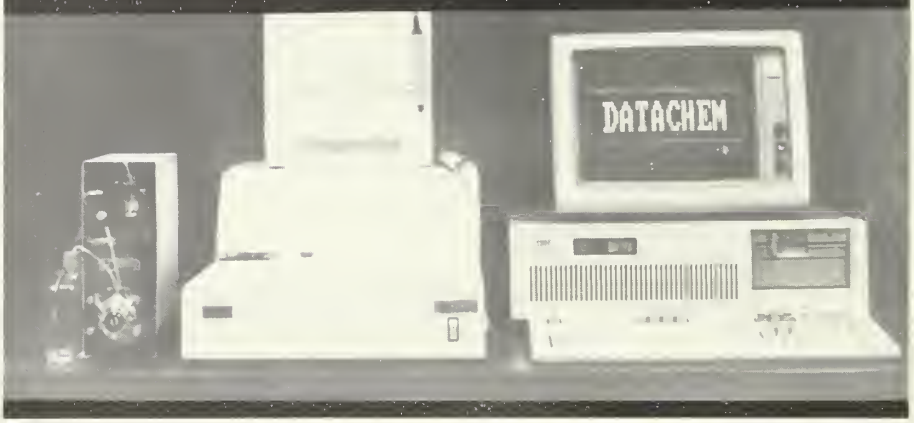
Dr. Khalouf presents a recognition plaque to Dr. Siebenmorgen.



Dr. Shirley Thompson Khalouf and her husband, Dr. Herbert C. Khalouf (left), pose with Dr. Paul Siebenmorgen (right) and his wife, Jane.

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Call to Order, Miscellaneous Business

The Indiana State Medical Association House of Delegates convened its 137th Annual Convention, featuring the theme "New Frontiers in Medical Care," at 1 p.m., EST, Thursday, Oct. 30, 1986, at the Hyatt Regency, Indianapolis. The final session of the House of Delegates convened at 9:30 a.m., EST, Sunday, Nov. 2, 1986. Presiding at both sessions were Dr. Fred Dahling, speaker, assisted by Dr. C. Dyke Egnatz, vice speaker. Dr. Lloyd L. Hill, Peru, served as parliamentarian.

Approval of Minutes

The proceedings of the 136th Annual Meeting of the House of Delegates, Indiana State Medical Association, conducted Nov. 14-17, 1985, at the Century Center, South Bend, Indiana, and published in the January 1986 issue of INDIANA MEDICINE, were approved.

Election of Officers

Dr. Shirley Thompson Khalouf, Marion, as president-elect, succeeded to the office of president. Dr. John MacDougall, Beech Grove, was elected president-elect. Other elections included:

Treasurer—Dr. George Rawls, Indianapolis

Assistant Treasurer—Dr. Max Wesemann, Franklin

Speaker of the House—Dr. Fred W. Dahling, New Haven

Vice Speaker of the House—Dr. C. Dyke Egnatz, Schererville

Chairman, Board of Trustees—Dr. Michael Mellinger, LaGrange

Clerk/Chairman Pro Tem, Board of Trustees—Dr. Benny Ko, Terre Haute

At Large Member, Executive Committee—Dr. William C. VanNess, II, Summitville

At Large Member, Executive Committee—Dr. William H. Beeson, Indianapolis

Election of Delegates, Alternate Delegates to the AMA

The following were elected to two-year terms as delegates and alternate delegates to the American Medical Association, their terms to expire Dec. 31, 1988:

Delegates:

Everett E. Bickers, M.D., Floyds Knobs

Alvin J. Haley, M.D., Carmel

John Knote, M.D., Lafayette

Alternates:

Edward Langston, M.D., Flora

George T. Lukemeyer, M.D., Indianapolis

Robert M. Seibel, M.D., Nashville

Holdover AMA delegates and alternate delegates (Terms expire Dec. 31, 1987):

Delegates:

Marvin E. Priddy, M.D., Fort Wayne

Peter R. Petrich, M.D., Attica

Thomas C. Tyrrell, M.D., Hammond

IN MEMORIAM

Tribute to members of the Indiana State Medical Association who have died since the 1985 session.

John E. Alexander, M.D., Evansville
Richard H. Appel, M.D., Indianapolis
Aaron L. Arnold, M.D., Indianapolis
Wendell W. Ayres, M.D., Marion
Henry G. Backer, M.D., Ferdinand
Elmer A. Barron, M.D., Hammond
Harvey L. Bartsch, M.D., Sun City, AZ (formerly of South Bend)
Margaret A. Bassett, M.D., Thorntown
Thomas B. Bauer, M.D., Sun City, AZ (formerly of Indianapolis)
Lavon D. Bechtol, M.D., Punta Gorda, FL (formerly of Indianapolis)
James G. Bledsoe, M.D., Naples, FL (formerly of New Castle)
Louis H. Blessinger, M.D., Corydon
Paul R. Boren, M.D., Poseyville
Edgar R. Cantwell, M.D., Vincennes
William B. Carr, M.D., Beaumont, TX (formerly of Fort Wayne)
Harold D. Caylor, M.D., Bluffton
Leroy B. Chambers, M.D., Union City
Edward E. Clark, M.D., Indianapolis
Harry M. Covell, M.D., Auburn
Alfred B. Coyner, M.D., Clarks Hill
Frederick A. Cravens, M.D., Indianapolis
Harry L. Craig, M.D., Huntingburg
Donald I. Dean, M.D., Sarasota, FL (formerly of Rushville)
Frederick R. Dettloff, M.D., Greencastle
William S. Dininger, M.D., Winchester
Stuart J. Duncan, M.D., Indianapolis
George W. Dyer, M.D., Terre Haute
Arthur N. Ferguson, M.D., Walnut Creek, CA (formerly of Fort Wayne)
J.N. Garber, M.D., Indianapolis
Charles F. Gillespie, M.D., Indianapolis
Douglas J. Giorgio, M.D., Evansville
Oscar Green, M.D., Indianapolis
Joseph P. Griffin, M.D., Chesterton
Harold J. Halleck, M.D., Winamac
Robert L. Haller, M.D., Kempton
Herbert P. Hargett, M.D., Jeffersonville
Carl J. Harmon, M.D., Richmond
Ralph Harvey, M.D., Zionsville
A.P. Hattendorf, M.D., Fort Wayne
Ellsworth K. Haugseth, M.D., South Bend
James H. Hawk, M.D., Indianapolis
Charles L. Herrick, M.D., Akron
Ralph L. High, M.D., Muncie
Jean F. Hinchman, M.D., Parker
Thomas A. Jean, M.D., Morristown
Leo Kammen, M.D., Indianapolis
Joseph E. Kopcha, M.D., Hobart
Ralph A. Lundeberg, M.D., N. Fort Myers, FL (formerly of Griffith)
John H. Machledt, M.D., Bargersville
Charles W. Magnuson, M.D., South Bend
Stephen D. Malouf, M.D., Lakeland, FL (formerly of Peru)
Howard H. Marks, M.D., Huntington
John M. Masters, M.D., Indianapolis
Harold L. Miller, M.D., Richmond
Floyd W. Mohler, M.D., Columbus
Jean W. Morris, M.D., Muncie
John B. Nicosia, M.D., East Chicago
Rufus M. Nigh, M.D., Flat Rock
John E. Owen, M.D., Carmel
Donald S. Painter, M.D., Fort Wayne
Alfredo Q. Paje, M.D., Indianapolis
Seymour L. Pollack, M.D., Indianapolis
Leo Radigan, M.D., Hammond
Donald T. Rendel, M.D., Hammond
Nancy C. Roeske, M.D., Indianapolis
James R. Roth, M.D., Columbia City
Lloyd O. Rupe, M.D., Elkhart
Robert B. Sanderson, M.D., South Bend
Irvin H. Scott, M.D., Sullivan
Hassi Shina, M.D., Louisville, KY (formerly of Charlestown)
John Slaughter, M.D., Evansville
Raymond E. Smalley, M.D., Meadowood
Bonnell M. Souder, M.D., Hobart
Martha C. Souter, M.D., Indianapolis
Joe W. Sovine, M.D., Indianapolis
Joseph H. Stamper, M.D., Anderson
Lucian A. Stamper, M.D., Richmond
Donald E. Stephens, M.D., Indianapolis
Wm. R. Storer, Sr., M.D., Indianapolis (formerly of Hobart)
Dorothy D. Teal, M.D., Columbus
John G. Trimble, M.D., Kokomo
William B. Triplett, M.D., (formerly of Evansville)
Isabel Turner, M.D., Evansville
Chester H. Warfield, M.D., Fort Wayne
William J. Warn, M.D., Milan
Irwin W. Wilkens, M.D., Indianapolis
Paul D. Williams, M.D., Indianapolis
Harold R. Wirey, M.D., Indianapolis
Henry L. Worley, M.D., New Albany
Dewey D. Yoder, M.D., Pierceton

Alternates:
Martin J. O'Neill, M.D., Valparaiso
Herbert C. Khalouf, M.D., Marion
Vincent J. Santare, M.D., Munster

Elected/Reelected Trustees, Alternates—1986-87

Trustees:
District 1—E. DeVerre Gourieux, M.D.
District 4—William E. Cooper, M.D.
District 7—John MacDougall, M.D.
District 10—Nicholas L. Polite, M.D.
District 13—Steven Yoder, M.D.

Alternates:
District 2—Jerome E. Melchior, M.D.
District 3—Gordon Gutmann, M.D.
District 4—George Alcorn, M.D.
District 6—Ray A. Haas, M.D.
District 9—R. Adrian Lanning, M.D.
District 10—Frank M. Sturdevant, M.D.
District 11—Jack Higgins, M.D.
District 12—Thomas Felger, M.D.
District 13—Alfred C. Cox, M.D.

Dr. Donna Meade, alternate trustee, District 7, succeeds to the office of trustee, District 7, due to the election of Dr. John MacDougall to the office of president-elect. According to the ISMA Bylaws, the president of the District Medical Society, Dr. John Records, Franklin, assumes the office of alternate trustee.

Scientific Exhibit Awards

First Place: "Neuromuscular Testing of the Stretch Reflex by Accelerometry."

Exhibitors: Larry K. Steinrauf, Ph.D., and James Pawlus, senior medical student, Indiana University School of Medicine.

Second Place: "Autologous Skeletal Muscle Pouch as a Cardiac Assist Device: Functional Analysis."

Exhibitors: Boyd C. Marts, B.C., J. Brown, M.D., K. Klueber, Ph.D., C. Rothe, Ph.D., R. Bills, B.S., and D. Gray, B.S., Indiana University School of Medicine.

Third Place: "Cytoarchitecture of Diabetic Muscle."

Exhibitors: John D. Feczko and Kathleen M. Klueber, Medical Sciences Program, Indiana University School of Medicine.

Dr. John MacDougall Chosen President-Elect

Dr. John D. MacDougall of Beech Grove was chosen president-elect of the Indiana State Medical Association Nov. 2 during the 137th annual convention in Indianapolis.

He was elected by the 200-member House of Delegates during the final session of the House. He will assume the presidency of the ISMA at its 138th annual convention in Indianapolis in November.

Dr. Shirley Thompson Khalouf of Marion succeeded Dr. Paul Siebenmorgen of Terre Haute as president.

Dr. MacDougall is engaged in the private practice of surgery and is an assistant professor of surgery at Indiana University School of Medicine. He earned a B.S. degree and the M.D. degree from Indiana University. He completed an internship and residency at the I.U. Medical Center. He is a diplomate of the American Board of Surgery and the American Board of Thoracic Surgery, and is a fellow of the American College of Surgeons.



Dr. MacDougall

Dr. MacDougall had been chairman of the ISMA Board of Trustees and a trustee of the Seventh District since 1983. He previously served as an alternate trustee, as chairman of the ISMA Commission on Medical Services, and as chairman of the ISMA Subcommission on Insurance. He was president of the Marion County Medical Society from 1978 to 1979.

Dr. MacDougall is a former president of the medical staff and chief of surgery of St. Francis Hospital, Beech Grove, where he is presently a member of the Advisory Board of Directors. He is a member of the active staff at University Heights Hospital in Indianapolis. In addition, he is a member of the Governor's Task Force on Organ Transplantation.



ISMA Welcomes Its 144th President

SHIRLEY THOMPSON KHALOUF, M.D.

President
Indiana State Medical Association
1986-1987

Dr. Shirley Thompson Khalouf of Marion accepted the presidency of the Indiana State Medical Association Nov. 2 during the final session of the House of Delegates at the 137th annual convention of the ISMA.

Dr. Khalouf, speaker of the House until November 1985, succeeded Dr. Paul Siebenmorgen of Terre Haute as president of the Association.

Dr. Khalouf is a board-certified private practitioner specializing in physical medicine, rehabilitation, electromyography and nerve conduction. She was formerly director of the physical medicine and rehabilitation department of Marion General Hospital; she is also a former chief of the medical staff and chief of medicine of the Marion hospital.

She earned a B.A. degree from Susquehanna University (Selinsgrove, Pa.) and the M.D. degree from the Medical College of Pennsylvania. After internships in Philadelphia and Harrisburg, she completed a residency at the Cleveland (Ohio) Clinic Foundation.

Dr. Khalouf is a member of the Indiana Commission for the Handicapped and serves on the Medical Advisory Board of the Grant County Visiting Nurse Association. She formerly served on the board of the Central Indiana Health Systems Agency. She was vice-speaker of the ISMA House of Delegates from 1980 to 1983. She has been a delegate from Grant County and has been a member of the ISMA Commission on Convention Arrangements. She is a former president of the 11th District Medical Society and of the Grant County Medical Society.

Dr. Khalouf is the first woman president of the ISMA, originally formed in 1849. Her professional affiliations include the American Congress Rehabilitation Medicine and the International Rehabilitation Medical Association.

She is married to Dr. Herbert C. Khalouf, a general surgeon who is presently an AMA alternate delegate. They have four children.

House of Delegates

COUNTY	DELEGATE	1ST SESSION	2ND SESSION
ADAMS (1)	Norval Rich	x	x
ALLEN/FT. WAYNE (9)	Charles Aust	x	x
	Frank Bryan	x	x
	Fred Dahling	x	x
	Thomas Felger	x	x
	Marvin Priddy	x	x
	M. Saferstein-Roszerman	x	x
	Charles Schoenhals	x	x
	Alan Sidel	x	x
	Harry Tunnell	x	x
BARTH/BROWN (3)	Richard Pittman	x	x
	Edward Probst		x
	Robert Seibel	x	x
	William Cooper	x	
BENTON (1)			
BOONE (1)	Dallas Coate	x	x
CARROLL (1)	T. Neal Petry	x	x
CASS (1)	Richard Glendening	x	x
CLARK (2)	Gordon Guttman	x	x
CLAY (1)			
CLINTON (1)	Stephen Tharp	x	x
DAVIESS/ MARTIN (2)	Horace Norton	x	
DEARBORN/ OHIO (2)	Gerald Bowen	x	x
	Frank Frable	x	x
DECATUR (1)			
DE KALB (1)	Mark Souder		x
DELAWARE/ BLACK (4)	Larry Cole	x	x
	John Osborne	x	x
	Donald Hunsberger	x	x
	L. Marshall Roch	x	x
DU BOIS (1)	Thomas Gootee	x	x
ELKHART (3)	G. Beach Gattman	x	x
	E. Larry Knight	x	x
	Max Mertz	x	x
FAYETTE/ FRANKLIN (2)	William Kerrigan	x	x
	Perry Seal	x	x
FLOYD (1)	Charles Carty	x	x
FOUNT/ WARREN (2)	Theodore Person	x	x
	Atee Salvo	x	x
FULTON (1)			
GIBSON (1)	William Wells	x	x
GRANT (2)	Laurence Musselman	x	x
	Herbert Khalouf	x	x
GREENE (1)	Frederick Ridge	x	x
HAMILTON (1)	R. Adrian Lanning	x	x
HANCOCK (1)	Ray Haas	x	
HARR/ CRAWFORD (2)			
HENDRICKS (1)	Lloyd Terry	x	x
HENRY (1)			
HOWARD (2)	Jack Higgins	x	x
	Tom Scherschel	x	x
HUNTINGTON (1)	Richard Wagner	x	x
JACKSON (1)	George Weir	x	x
JASPER (1)			
JAY (1)	James Fitzpatrick	x	x
JEFF/SWITZ (2)	George Alcorn	x	x
JENNINGS (1)	Thomas Barley		x
	Larry Brooks	x	
JOHNSON (1)	Max Wesemann	x	x
KNOX (1)	Jerome Melchior	x	x
KOSCIUSKO (1)	Wymond Wilson	x	x
LA GRANGE (1)	John Egli	x	x
LAKE (13)	Thomas Brubaker	x	x
	J. Albert Carey	x	x
	Mary Carroll	x	x
	C. Dyke Egnatz	x	x
	Frank Hieber	x	x
	P. G. Iatridis	x	x
	Walfred Nelson	x	x
	Barron Palmer	x	x
	Daniel Ramker	x	
	William Sabo	x	x
	Joseph Sala	x	x
	Lee Trachten-berg	x	x
	Thomas Tyrrell	x	x
	George Volan		x
LA PORTE (2)	Barbara Backer		x
	David Miller	x	x
LAWRENCE (1)	Richard Huber	x	x
MADISON (3)	Joseph Copeland	x	x
MARION (32)	Ronald Blanken-baker	x	x
	Bryan Burney	x	x
	Edward Cockerill	x	
	Helen Czenkusch	x	x
	Bernard Emkes	x	
	A. Alan Fischer	x	x
	Bradford Hale		x
	Jack Hall		x
	Jerry House		x
	Donald Kerner	x	
	Stephen Jay	x	x
	James McCallum	x	
	Loren Martin	x	x
	B. T. Maxam	x	x
	Donna Meade	x	x
	I. E. Michael	x	x
	Robert Mouser	x	x
	David Need	x	x
	John Pantzer	x	x
	Robert Parr		x
	George Rawls	x	x
	Carl Ray	x	x
	Donald Rogers		x
	Robert Rudesill		x
	Barton Rusk		
	Roland Rust	x	x
	Donald Schlegel	x	x
	Richard Schnute	x	x
	John Smith	x	
	Willis Stogsdill	x	x
	Jamie Street		x
	H. Marshall Trusler		x
	Virginia Wagner	x	
	Douglas White	x	x
MARSHALL (1)			
MIAMI (1)	Rhys Jones	x	x
MONTGOMERY (1)			
MORGAN (1)			
NEWTON (1)			

House of Delegates

COUNTY	DELEGATE	1ST SESSION	2ND SESSION
NOBLE (1)			
ORANGE (1)			
OWEN/MONROE (4)	B. Diane Wells	x	x
	William Weber, Jr.	x	x
	David Johnloz	x	x
PARK/VERM (2)			
PERRY (1)	Robert Ward		x
PIKE (1)			
PORTER (2)	Frank Sturdevant	x	x
	John Swarner, Jr.		x
POSEY (1)	John Vogel		x
PULASKI (1)			
PUTNAM (1)	Fred Haggerty	x	x
RANDOLPH (1)	Susan Pyle	x	x
RIPLEY (1)	Manuel Garcia	x	x
RUSH (1)	Davis Ellis	x	x
ST. JOSEPH (6)	Don Chamberlain	x	x
	Alfred Cox	x	x
	Robert Dodd	x	x
	G. Richard Green	x	x
	Richard Schaphorst	x	x
	Lee Smith	x	
SCOTT (1)	Jesus Bacala	x	
SHELBY (1)	Wilson Dalton	x	x
SPENCER (1)			
STARKE (1)	Walter Fritz		x
STEUBEN (1)	Kenneth Bison	x	x
SULLIVAN (1)			
TIPPECANOE (4)	Dennis Richmond	x	x
	Kyle Loy		x
	Paul Maier	x	x
	George Underwood	x	x
TIPTON (1)			
VANDERBURGH (8)	John Beman		x
	John Bizal		x
	Charles Hachmeister	x	x
	Eugene Hendershot		x
	Bruce Romick	x	x
	L. Ray Stewart		x
VIGO (3)	William Strecker	x	x
	Robert Taube		x
WABASH (1)	James Haughn	x	x
WARRICK (1)	Syed Ali		x
WASHINGTON (1)			
WAYNE/UNION (3)	James Daggy	x	x
	John Hinton	x	x
	James Lewis	x	x
WELLS (1)	Wallace Van den Bosch	x	x
WHITE (1)			
WHITLEY (1)			
STUDENT DELEGATE (1)	Anita Spitz	x	x
RESIDENT DELEGATE (4)	Mark Bradley	x	
	Lana Patch	x	x
	Silvio Garcia	x	x
	James Jennison	x	x
	Michael Williams		x

Reference Committees

REFERENCE COMMITTEE NO. 1
Reports of Officers
*William C. VanNess II, M.D., Summitville
William F. Kerrigan, M.D., Connersville
David J. Need, M.D., Indianapolis
William Strecker, M.D., Terre Haute
Paul Honan, M.D., Lebanon
Alfred Cox, M.D., South Bend

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Constitution and Bylaws
*William Sabo, M.D., Munster
Rhys D. Jones, M.D., Peru
William R. Wells, M.D., Princeton
George Weir, M.D., Brownstown
Max Wesemann, M.D., Franklin
Charles H. Aust Sr., M.D., Fort Wayne

REFERENCE COMMITTEE NO. 3
Legislation
*Donald Kerner, M.D., Indianapolis
Donald S. Chamberlain, M.D., Mishawaka
Frank M. Sturdevant, M.D., Valparaiso
B. Diane Wells, M.D., Spencer
Charles E. Schoenhals, M.D., Fort Wayne
Susan K. Pyle, M.D., Union City

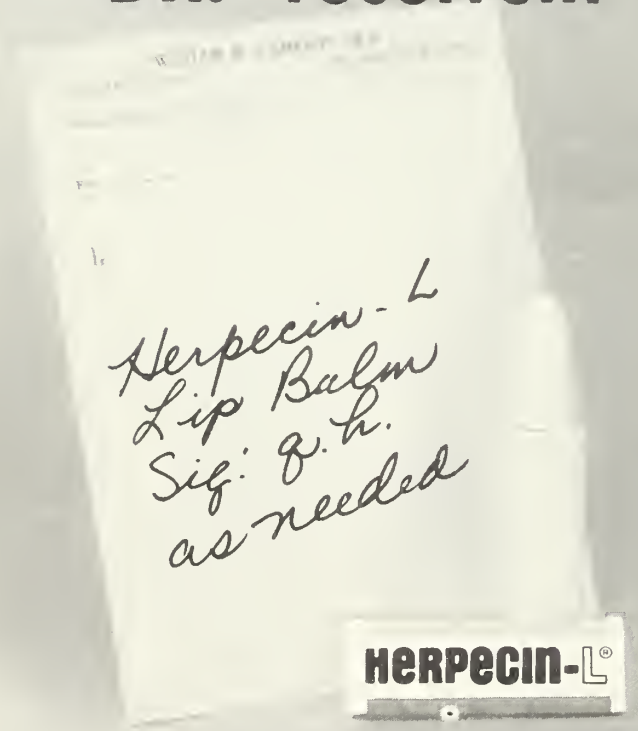
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Medical Education and Insurance
*Thomas A. Felger, M.D., Fort Wayne
John Bizal, M.D., Evansville
Stephen D. Tharp, M.D., Frankfort
William Beeson, M.D., Indianapolis
Wymond Wilson, M.D., Mentone

REFERENCE COMMITTEE NO. 5
Miscellaneous
*Harry D. Tunnell, M.D., Fort Wayne
Mark S. Souder, M.D., Auburn
Virginia Wagner, M.D., Indianapolis
Paul Wenzler, M.D., Bloomington
Eva Fadul, Indianapolis
Douglas White, M.D., Indianapolis

REFERENCE COMMITTEE NO. 6
AMA Matters
*John Egli, M.D., Topeka
Daniel T. Ramker, M.D., Hammond
Everett E. Bickers, M.D., Floyds Knobs
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Mark Bradley, M.D., Indianapolis
Tom Scherschel, M.D., Kokomo

*Chairman

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Status of 1985 Resolutions

The following summary is submitted as a Supplement to the Annual Report of the Chairman, Board of Trustees:

RESOLUTION 85-1 DESIGNATED TAX ON ALCOHOL AND TOBACCO PRODUCTS
Introduced by: Resident Medical Society of Indiana
Referred to: Commission on Medical Education
Status: Accepted for information

RESOLUTION 85-2 MEMBERSHIP OF ACTIVE DUTY MILITARY PHYSICIANS
Introduced by: Miami County Medical Society
Referred to: Board of Trustees with subsequent report to the 1986 House of Delegates
Status: See Resolution 86-8

RESOLUTION 85-3 LEGAL NEGOTIATIONS WITH THIRD PARTY PAYORS
Introduced by: Miami County Medical Society
Referred to: Commission on Medical Services
Status: Continuing activity of ISMA

RESOLUTION 85-4 FUNDING FOR GRADUATE MEDICAL EDUCATION
Introduced by: Commission on Medical Education
Referred to: Commission on Legislation
Status: Copy of Resolution referred to members of the Indiana Congressional Delegation

RESOLUTION 85-5 NOT ADOPTED

RESOLUTION 85-6 NOT ADOPTED

RESOLUTION 85-7 NOT ADOPTED

RESOLUTION 85-8 ISMA MEMBERSHIP SUSPENSION AS A RESULT OF MEDICAL LICENSING BOARD SUSPENSION
Introduced by: Commission on Physician Impairment
Referred to: Board of Trustees
Status: See Resolution 86-44

RESOLUTION 85-9 NOT ADOPTED

RESOLUTION 85-10 NOT ADOPTED

RESOLUTION 85-11 THERAPEUTIC AND PHARMACEUTICAL SUBSTITUTION BY PHARMACISTS
Introduced by: AMA Delegation and Board of Trustees
Referred to: 1. AMA House of Delegates
2. Commission on Legislation
Status: 1. Implemented
2. No bill was filed for consideration in the 1986 Indiana General Assembly. The Legislative Department will monitor this issue closely at the Indiana Legislature.

RESOLUTION 85-12 NOT ADOPTED

RESOLUTION 85-13 PHYSICIANS TO SERVE AS FULL VOTING MEMBERS ON HOSPITAL BOARDS OF TRUSTEES
Introduced by: ISMA-HMSS
Referred to: Commission on Legislation
Status: Legislation was introduced, however, died in the House.

RESOLUTION 85-14 NOT ADOPTED

RESOLUTION 85-15 ABUSE OF PEER REVIEW MECHANISMS
Introduced by: Joe Richardson, M.D.
Referred to: Commission on Medical Services
Status: Referred to HMSS. HMSS will consult further with legal counsel and assess recommendations from the AMA 1987 Interim Meeting for a report back to the ISMA Board of Trustees.

RESOLUTION 85-16 UNIFORM DETERMINATION OF DEATH ACT
Introduced by: Commission on Legislation
Referred to: Commission on Legislation
Status: Implemented (PL 1-1986)

RESOLUTION 85-17 MOTORCYCLE HELMETS
Introduced by: Commission on Legislation
Referred to: Commission on Legislation
Status: Implementing

RESOLUTION 85-18 A SMOKE-FREE SOCIETY BY THE YEAR 2000
Introduced by: Commission on Legislation
Referred to: Commission on Legislation and Public Relations
Status: Implementing

RESOLUTION 85-19 NOT ADOPTED

RESOLUTION 85-20 BREAST CANCER INFORMATION
Introduced by: Richard G. Huber, M.D.
Referred to: Commission on Public Relations
Status: Implemented

RESOLUTION 85-21 RECOMMENDATIONS TO INDIANA LEGISLATURE
Introduced by: Commission on Sports Medicine
Referred to: Commission on Sports Medicine
Status: Being implemented

RESOLUTION 85-22 .05% BLOOD ALCOHOL CONCENTRATION AS PER SE ILLEGAL FOR DRIVING
Introduced by: Reduce Drunk Driving Committee
Referred to: Commissions on Legislation and Public Relations
Status: Legislation was introduced, however, was not granted a committee hearing.

RESOLUTION 85-23 HOSPITAL MEDICAL STAFF SECTION
Introduced by: Commission on Constitution and Bylaws
Referred to: Commission on Constitution and Bylaws
Status: Implemented

RESOLUTION 85-24 UPDATING OF THE ISMA CONSTITUTION TO BE IN COMPLIANCE WITH RECENT CHANGES TO THE ISMA BYLAWS
Introduced by: Commission on Constitution and Bylaws
Referred to: Commission on Constitution and Bylaws
Status: Implemented with approval by 1986 House of Delegates

RESOLUTION 85-25 AMENDMENTS TO BYLAWS AS A RESULT OF THE PASSAGE OF RESOLUTIONS 84-8 AND 84-9 DEALING WITH RESIDENT MEDICAL SOCIETY REPRESENTATION ON THE ISMA BOARD OF TRUSTEES AND ISMA HOUSE OF DELEGATES
Introduced by: Commission on Constitution and Bylaws
Referred to: Commission on Constitution and Bylaws
Status: Implemented

RESOLUTION 85-26 AD HOC STUDY COMMITTEE ON FIELD STAFF MEMBERSHIP SERVICES
Introduced by: Lawrence E. Allen, M.D., F.A.C.S.

Status of 1985 Resolutions

Referred to: Future Planning Committee
Status: Being implemented through Strategic Planning Process

RESOLUTION 85-27 PHYSICIAN SUPPORT SERVICES
Introduced by: Lawrence E. Allen, M.D., F.A.C.S.
Referred to: Commission on Medical Services
Status: To be implemented in FY 86-87

RESOLUTION 85-28 AD HOC STUDY COMMITTEE ON HEALTH CARE FOR THE INDIGENT IN INDIANA
Introduced by: Lawrence E. Allen, M.D., F.A.C.S.
Referred to: Executive Committee, ISMA President and for Report back to 1986 House of Delegates
Status: Implemented

RESOLUTION 85-29 AD HOC STUDY COMMITTEE, AIDS PROGRAM
Introduced by: Lawrence E. Allen, M.D., F.A.C.S.
Referred to: ISMA President
Status: Implemented

Report of the Chairman, Board of Trustees
John D. MacDougall, M.D., Chairman
Referred to: Reference Comm. 1
ACTION: Filed
(Report was published in the October 1986 issue of INDIANA MEDICINE)

Report of the Chairman, Executive Committee
Paul Siebenmorgen, M.D., Chairman
Referred to: Reference Comm. 1
ACTION: Filed
(Report was published in the October 1986 issue of INDIANA MEDICINE)

Report of the Editor, INDIANA MEDICINE
Frank R. Ramsey, M.D.
Referred to: Reference Comm. 1
ACTION: Filed
(Report was published in the October 1986 issue of INDIANA MEDICINE)

Report of the Treasurer
George H. Rawls, M.D., Treasurer
Max Wesemann, M.D., Asst. Treas.
Referred to: Reference Comm. 1
ACTION: Referred for audit

Reports of Trustees
Referred to: Reference Comm. 1
ACTION: Filed
(Reports were published in the October 1986 issue of INDIANA MEDICINE)

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Address of the President

Paul Siebenmorgen, M.D.
Referred to: Reference Comm. 1
ACTION: Filed

Two years ago, this House elected me to become president of ISMA after I had served six years on the Board of Trustees, the last three years as Chairman of the Board and as a member of the Executive Committee. I stated in my acceptance remarks to this House of Delegates at that time that I counted it a most distinguished honor to be elected president of ISMA and I thanked the House for bestowing that honor on me. Then I stated I also knew that with that honor came huge, awesome responsibilities. I was willing to accept them and would discharge the duties of the office of president of ISMA to the very best of my abilities. Now, without reservation, I can say that I have done that. Time and history will judge the wisdom of this year after weighing the accomplishments and progress of our association. I really feel that that judgment will be favorable.

I was inaugurated as president a year ago succeeding Dr. Lawrence E. Allen who put together a year of masterful leadership, a difficult act to follow.

Complicating what I perceived to be a difficult task was a second major unsettling event. Don Foy, our able CEO of ten years, quietly announced to me during last year's House of Delegates meeting that he had tentatively accepted a similar position in New York and would be moving.

A third major concern was the decision being made to move our ISMA headquarters from its present location.

With these problems of such magnitude facing me, I took a deep breath, tightened my belt, and with determination to succeed, I asked for God's guidance and started my year of leadership along with our new president-elect, new chairman of the Board, new speaker and new vice-speaker of the House.

First, the Board of Trustees approved the Search Committee, with me as chairman, to seek and find a new executive director. Through national advertisement, the process was begun and Ken Bush was recalled to full-time service from partial retirement to be our acting executive director. With great cooperation from our excellent staff who were willing to go the extra mile, work continued very much in its usual efficient manner.

When our new executive director, Rick King, was finally selected and after taking office in April, it seemed an appropriate time to set some new goals for ISMA.

Thus, virtually all summer, members of the Future Planning Committee met to analyze what ISMA has done in the past as well as examine the changing medical environment we currently face. Initially, they scheduled several focus groups around the state. Some of you participated in these meetings which were designed to seek your comments.

With the help of the Health Policy Research Group acting as an analyst and facilitator, the Future Planning Committe has worked very hard in lengthy sessions to review the information. While that process is not quite finished, it is nearing completion. I want to commend the Future Planning Committee and its chairman, Dr. William VanNess, for undertaking this complex and very time-consuming project. The committee will soon finish their work and, at an appropriate time, will present their recommendations to the Board of Trustees and subsequently to the county and district officers for their information, comments and implementation.

Usually, the text of the president's address includes a considerable portion on future activities. I shall defer such comments and acquiesce to that Long Range Planning Committee's report soon to be released. I have been an active participant at all the committee's activities and am enthusiastic about the potential benefits of its proposals. I urge you each to study it carefully when it is available.

While the final report will provide us with direction for the future, there are three endeavors that I feel are particularly important to the Indiana State Medical Association currently and must be sustained. First are our important legislative efforts; second, is our new direction in regard to public affairs; and, third, is our continued advocacy for quality health care.

We are fortunate at ISMA to have tremendously experienced people on our legislative staff. ISMA's Key Contact program is one of the best organized in the country. Within a brief interlude, Key Contact physicians and auxilians across the state can be alerted about an issue or a vote pending in the Congress or in our Indiana General Assembly. How much more efficient such a system could be if each legislator could have a hundred physician contacts instead of our two or three. Is it too much to ask each one of you to respond? It is your business to furnish the proper, appropriate health care to the people of our state. Legislators must be informed on these issues.

This year, you as members of ISMA's House of Delegates will be asked to support several legislative proposals. One of the most important is in keeping with our increased emphasis on public affairs, specifically our Tobacco-Free Society campaign. As you all recall, the 1985 House of Delegates endorsed Resolution 85-18, a proposal to work for a tobacco-free society in concert with the American Medical Association's initiative on the same issue.

Smoking kills more Americans than any other personal health habit or any other environmental hazard. I don't mean to preach to the choir here. We are physicians. We have seen the pain and suffering, the blackened lungs, the cancerous lungs, the hardened arteries, the damage to newborn babies. If the personal pain is not enough reason for publicly urging people to stop using tobacco, consider the cost to our society. Adverse effects of smoking cost the U.S. an average of $65 billion per year in higher medical bills, premature death, and time off from work, according to a congressional study reported in 1985.

Following the directive of the 1985 House of Delegates, our Commissions on Legislation and Public Relations authorized staff to form the Indiana

Coalition for a Tobacco-Free Society. The Coalition so far is made up of representatives from 20 organizations and other individuals who share our concern about the health hazards of tobacco use.

This House will be asked to approve several measures to promote a tobacco-free society. Legislative proposals like this and others named in resolutions will first be considered in reference committees and I invite your participation.

A few moments ago, I mentioned our advocacy of quality health care. I particularly include in that quality health care for older people, the fastest growing segment of our population.

The AMA adopted a proposal for financing health care of the elderly at its meeting in June. While it is too lengthy to discuss here, I will say, however, that it would provide a prefunded program, comprehensive protection, including catastrophic coverage and a voucher system to allow the beneficiary a choice of coverage. Also, it would allow additional contributions to IRAs for funding supplemental elderly health care expenses. Our association will be called upon to discuss and debate the proposal with policy makers, physicians, and Medicare beneficiaries in an effort to solve the Medicare crisis we now face. ISMA must remain dedicated to efforts in this arena and we must continue to meet with concerned groups such as the Indiana Federation of Older Hoosiers, to talk about common concerns.

Now, after discussing these three major concerns and our strategic planning process, I'd like to shift gears and call your attention to last year's address of the president-elect. In that address, I stated that as a consequence of the realization that the environment of medicine will continue to be altered, and with the realization that we must function wisely to ensure the continued growth and viability of ISMA, I intended, during my tenure, to continue strong emphasis in nine main areas.

I am proud to say to this House that our Association has done that with diligence, in addition to the ISMA activities already mentioned here, and others. First, there has been an excellent emphasis on membership development with continuing emphasis on communications with members, and a positive public relations program. A third field staff person was added to assist in these areas and a concerted effort by the President and all our staff members has resulted in our membership reaching an all-time high of 6,599. A significant impact on that number also came from ISMA membership being a requirement before physicians could participate in advantageous insurance programs and certain HMOs such as Firstcare and Physicians Medical Alliance.

Also developed this year was an ISMA Physicians Service Department under the directorship of Mike Huntley. ISMA now offers some 20 financial services from automobile purchase to bank charge cards to accounting service arrangements. Of course, ISMA still offers its advantageous group health insurance through Lincoln National and that very important professional liability and indemnity coverage through the Physicians Insurance Company of Indiana (PICI). Our American Physicians Life Insurance Company (APL) offers excellent rates for our members, a wide range of life insurance and retirement plans, and other financial services.

Adequate housing arrangements for ISMA have been made at our present location at 3935 North Meridian Street. Under the present plan, there will be enough parking area, meeting facilities and comfortable room for our staff, as well as a small park for outdoor activities for small groups and families. Our continuing support of the programs of our commissions and committees has produced many successes that will be reported to you during this meeting. I have already mentioned the exemplary work of the Legislative, Medical Services, and Public Relations Commissions and the Long Range Planning Committee, but so has been the work of the Sports Medicine, Impaired Physicians, Medical Education, and Convention Arrangements Commissions.

The father of the doctor chairing our Convention Arrangements Commission this year was my classmate in many undergraduate courses at Indiana State University and was my roommate during my first semester of medical school, the late Dr. Jack Glosson. And so, you see, his daughter, Dr. Diane Wells, is somebody special to me and I appreciate her excellent leadership this year as the Chairman of the Convention Arrangements Commission.

The Resident and Medical Student Component Medical Societies have grown in stature, numbers, and programs this year and our new Hospital Medical Staff Section has blessed us with a model medical staff bylaws after many meetings throughout the year. I encourage all hospital medical staffs to study this model document for their own information and possible action.

No report of ISMA could be complete without mentioning and giving credit to our "partners in health," our auxiliary. Presidents Muriel Osborne and Alfrieda Mackel have been great leaders. Auxiliary membership is up. The auxiliary has been involved in developing our AMA-ERF funds for our medical school support, our Key Contact system for legislative efforts, our public relations activities through its program "An Early Start to Good Health," our membership awareness and development, and in many other ways. It is with this in mind that I submitted the resolution to get additional funds through our dues to more adequately support their programs.

In conclusion, ISMA has followed the course set before it. It is a responsive, healthy organization. Its membership is at an all-time high and it has a new Executive Director. The auxiliary, likewise, has grown and is vital and helpful. Strategic planning is nearing completion. Housing needs are fulfilled. Our legislative staff, Legislative Commission and IMPAC are producing at peak performance to be effective in the next legislature. PICI has a new CEO and a new president.

Ahead lies the future with changing times experienced yet by no one, but there is no doubt that with continuing

Address of the President

determination and dedication, ISMA can continue to accomplish its mission that has been so beautifully spelled out in our constitution and bylaws.

Dr. Malcolm Watts, in an editorial published recently in the AM News was exactly right when he said, "What is needed now is for practicing physicians and the medical profession to resurrect the human and caring aspects of their great calling—and make medical science and technology, and the social, economic and political forces that are so evident today, their servants in this cause and not let them be the masters."

I want to express my sincere thanks to you, the members of the Indiana State Medical Association, for allowing me the great honor of serving as your president. I thank Dr. Larry Allen, past-president, for his counsel. I also wish to extend my appreciation to Dr. John MacDougall, chairman of the Board, and to the Board of Trustees for their support, wisdom and good judgment in setting the course for ISMA.

I thank also the commissions and committees for their consistent contributions to our association. Additionally, ISMA Executive Director, Rick King, and his staff deserve special recognition.

To my colleague, Dr. Shirley Khalouf, I extend my best wishes for a rewarding year. Many times during my term Shirley graciously and ably filled in for me when scheduling conflicts arose. I appreciated her generous support and pledge mine to her.

Our members and the patients they serve are the better because of the dedication of *all* these people.

Before closing I wish to publicly thank my partner and associate, my daughter—Dr. Susan Amos, for minding the office and caring for my patients while I devoted more of my energies to ISMA. And, finally, I offer my profound appreciation to my lovely wife, Jane. She has been an exemplary first lady of ISMA this year who has traveled the many miles with me. Not just the miles this year, but during every year that I have had the pleasure of being a part of ISMA. She, too, endured the long hours, the late nights, some shaky airplane trips, and the hours of loneliness during my preparation . . . but her support, encouragement, and love make it all happen and all worthwhile.

Address of the President-Elect

Shirley Thompson Khalouf, M.D.
Referred to: Reference Comm. 1
ACTION: Filed

Thank you and good afternoon. The other day a quote was brought to my attention and it seems to describe the situation in which this country's medical profession finds itself . . . "The future isn't what it used to be."

Certainly as my term as President of the Indiana State Medical Association has drawn nearer, I have reflected on the future. It occurs to me that no matter how many changes we are faced with in medicine today, some things never change.

For example, the importance of belonging to organized medicine; and another is the need for us, the physicians, to continue to be advocates for our patients.

There are three main reasons for our active participation in organized medicine:

First, organized medicine provides information, not just on clinical aspects of medicine, but about socio-economic aspects of medicine.

Second, organized medicine provides us a mechanism to have impact on the laws and regulations governing the practice of medicine—something that is increasingly important as both government and business threaten to make cost, not quality, the determining factor in the delivery of medical care.

Third, through organized medicine we can exchange ideas with colleagues both inside and outside of our specialty areas.

As competition in the delivery of medical care becomes more prominent, its threat to the solidarity of organized medicine becomes more apparent.

Recently, I had the pleasure of hearing Dr. James Todd, senior deputy executive vice president of the AMA. Dr. Todd commented that things are so different now, it makes doctors fearful. He said we can't fight turf battles among ourselves ... we must pull together.

We would do well to heed his words.

The bottom line is and always has been that we must continue patient advocacy. No matter what our practice specialty; no matter whether we are hospital-based or in private practice; or whether we are fee for service or salaried physicians, we all share a responsibility to offer the best possible care to our patients.

We don't just do this in the hospital operating room, the outpatient clinic, or in our office examining rooms ...

We have to carry advocacy of our patients to Congress and to the Indiana General Assembly, as well.

Recently, the officers of ISMA visited several members of Indiana's Congressional delegation in Washington, D.C.

During our meeting with one Representative in Congress, we discussed several issues of concern.

What impressed me, however, was the congressman's questions for us regarding problems with IMRO, about which some of his physician/constituents had written to him.

What this said to us is that if our congressmen get enough letters, they do pay attention.

Part of the way we also carry our message is by voting. During this week

Address of the President-Elect

before election day, I think it would be most appropriate for you to review your state legislators' and your congressman's voting records and vote accordingly.

In these few short minutes, I've tried to outline for you why belonging to organized medicine is important ... and why we must continue to work on behalf of our patients.

I believe the key to each of these is communication. I would like to challenge each of you as members of the ISMA House of Delegates to use your positions as delegates to inform your county medical societies.

If each of you informed your county society members about just one issue currently facing them, just think what impact that could have.

Perhaps the future isn't what it used to be. Many of us are fearful about the future. New ventures and patterns in the practice of medicine are and will be in front of us.

We must meet those challenges objectively and we must be optimistic, not pessimistic, about the future of medicine. We must not permit outside forces to cause us to divide among ourselves, or to make us so fearful that we give up on this profession itself.

Again, perhaps the future isn't what it used to be, but if we work together we can still maintain a beautiful and fulfilling profession, and we can still maintain the highest quality medical care for our patients that the world has ever known.

Address of the President, ISMA Auxiliary

Alfrieda Mackel

Referred to: Reference Comm. 5
ACTION: Filed

Thank you for giving me time on your busy agenda to report on the medical auxiliary.

I have considered it a great honor and privilege to be a Partner in Health for forty-two years with one who has devoted his life and skills to the practice of medicine. I believe that you and your partners share this feeling of pride and commitment to providing quality health care in our Indiana communities. We share a common bond for a very noble purpose.

It is to this purpose that the medical auxiliary gives its time and energy and sets its goals.

We have a strong and unique partnership of 80,000 auxilians organized nationally in the AMA Auxiliary and over 2,500 organized in Indiana in 38 county auxiliaries, all working together to meet these goals. The ISMA Auxiliary Board of 28, representing all areas of the state, coordinates the efforts of this partnership.

Among the programs and projects of the auxiliary are:

- Raising funds for medical schools and for medical student assistance. Last year the auxiliary raised over two million dollars for AMA-ERF, of which the I.U. Medical School received the largest grant in the nation—over $75,000.
- Providing health scholarships to nurses and other medical related careers.
- Supporting good health legislation.
- Taking health education programs into schools; such as, a puppet show on child abuse and using the American Cancer Society Curriculum, "An Early Start to Good Health."
- Teaching CPR.
- Working in coalition with other groups to conduct health fairs, blood drives, meals-on-wheels, etc.
- Sponsoring education programs on stress, impairment, breast exams and many others.

It is always a highlight of our annual state meeting to hear the reports on counties' health projects and on the many ways of raising funds for their projects.

The ISMA Auxiliary Board works closely with the AMA Auxiliary to promote the use of their publications on health information, legislative issues and medical concerns. Leaders of the board organize delegates to the annual AMA Auxiliary House of Delegates and county leaders to national workshops.

By means of communication by letters, telephone calls and visits, officers and committee chairmen of the Board provide information, guidance and leadership to county auxiliaries.

Because we think it so important for auxilians to be knowledgeable on medical issues of concern to physicians, we have conducted two state workshops on program planning, and on medical issues, and leadership skill development with time for sharing of concerns and ideas. There will be a third workshop in April on a medical concern.

Much attention is given to increasing membership and membership participation by the auxiliary in order to make our organization stronger and more effective. This year for the first time a male auxilian is on our Board to tackle the male spouse membership potential. At the request of the AMA Auxiliary president, Pat Durham, he was asked to participate in a national workshop, Leadership Confluence-I, recently in Chicago. We also try to involve medical students' and residents' spouses and members at large (where there is no organized county auxiliary) in our programs. We also keep trying to organize additional county auxiliaries.

There is a close relationship between medical societies and medical auxiliaries in most of our county auxiliaries. This makes our programs more effective. Dr. Siebenmorgen and the other physicians of the medical society have been extraordinarily kind and complimentary to me personally. I keep humble by reminding myself it's the office not me they're praising and appreciating. I look forward to completing my year's program working

Address of the President, ISMA Auxiliary

closely with Dr. Khalouf.

We owe much to the ISMA staff. Richard King, Adele Lash, Julie Newland, Howard Grindstaff and others are much appreciated.

Our biggest help and the one who really keeps all our wheels turning smoothly is Rosanna Iler—liaison with the ISMA. Thank you very much for her services.

Serving as president of the ISMA Auxiliary is a challenge and a very high honor to me, and I thank you for the opportunity for doing good. I pledge my best effort to making Auxiliary your Partner in Health.

Address of the President, Medical Student Society

Robert S. Flint II

Referred to Reference Comm. 5
ACTION: Filed

I am very pleased to have the opportunity to bring the members of the ISMA up to date on the status and activities of the student population and the Medical Student Society at the Indiana University School of Medicine.

In regard to the general student population, the medical students continue to dominate the student government of the entire IUPUI Campus. This was a trend which began last year when medical students captured the vice-presidency and the majority of senate positions. This year medical students continue to prevail in the senate. I believe this indicates a desire on the part of the medical student to become involved in issues which affect the general population and which exist outside the realm of medical care. In addition, several significant changes in the physical structure of the campus are occurring. The new wing of Riley Children's Hospital has just been opened with new facilities in which medical students will be performing varied clinical duties. All of the students are anxiously awaiting the new library/research facility which is to be constructed behind the Medical Science Building. Ground breaking for this project is to take place in 1987.

The Medical Student Society is active at many levels. On the Medical Center Campus, we participated in the Freshman Orientation Program at the beginning of the school year with a booth at which we talked to the new students about their opportunities in organized medicine. We also carried out the disbursement of the AMA Drug Evaluation's Handbook on campus. These two events generated considerable interest in the medical student organizations at both the local and national levels. In addition, the Medical Student Society in cooperation with the ISMA began sponsoring a lecture series last Spring. The lectures are held twice yearly at lunchtime in one of the campus auditoriums. Last Spring, Hal Hefner, the Executive Director of the MCMA, presented some basic concepts related to alternative health care systems. Future presentations will include issues in medical law, ethics, medical practice opportunities, and obtaining residency.

At the county level, our new vice-president, Jon Finley, as part of the responsibilities of this office, is representing the medical students at the MCMA meetings. We hope to become more involved with activities and committees on the county level as our medical student organization develops.

At the state level, the medical students continue to be very active. At this ISMA meeting, our delegates Anita Spitz and Marty Ross are representing the medical students at the general assembly. Another medical student, Eva Fadul, is participating on a reference committee. In addition, many of our other active members are attending to observe the meeting. We also continue to participate on various state committees including Mary O'Conner on Sports Medicine, Cheryl McDonald (our Sec./Tres.) on Impaired Physicians and Public Relations, Jon Finley on Legislation, and Bob Flint, Rick Blackburn, and Kevin Ault on the Editorial Board of INDIANA MEDICINE.

At the national level, we took seven students to the AMA-MSS meeting at Chicago in June. Our delegate, Anita Spitz, served on the Credentials Committee and was also elected to the Nominating Committee for the student member of the AMA Board of Trustees. Eva Fadul participated as Chairman of the Rules Committee. Frequent testimony by the Indiana delegation had obvious impact on the ultimate decisions regarding many resolutions under consideration. In addition, the AMA-MSS allows one student delegate per medical school at the national meetings. Since the medical student population in most states is divided among more than one medical school while a comparable number of students in Indiana attend one school, the issue of underrepresentation in Indiana has been raised by prior IU delegates. At the June meeting, a committee specially appointed to evaluate this problem reported a plan to attempt to normalize representation, but this was rejected as too complex. There is now some suggestion of allowing Indiana University one or two more delegates. More specific details regarding the solution of this controversy will be elaborated at the December meeting. Finally, the IU Medical Student Society is developing closer contact with societies of the neighboring states including discussion of possible regional activities beyond the national conventions.

Last year was the first year of existence for the IU Medical Student Society, and during that time, we concentrated on development of internal organization and increased participation on state and national levels.

Address of the President, Medical Student Society

Our goals for the present and near future include increasing local organization to involve representation of each regional campus at semi-annual state medical student society meetings. In addition, we intend to strengthen recruitment locally in order to obtain members who desire to be active participants in the organization; therefore, we will direct efforts more toward quality than quantity of membership. Finally, we would like to increase our activities such as service projects directed toward medical students and the community in general.

Before concluding, I would like to extend a special thanks on behalf of all the members of the Medical Student Society to an individual who has worked very hard to help us start and now maintain this organization, Ms. Rosanna Iler. In addition, the Medical Student Society would also like to express our appreciation to the ISMA for allowing us a chance not only to learn but also to begin contributing in areas of medicine beyond clinical practice.

Report of the Resident Medical Society

Submitted by: John Terry, M.D., President
Referred to: Reference Comm. 5
ACTION: Filed

The Resident Medical Society began its third year in July of 1985 with strong momentum after conducting another successful "Welcome to the Practice of Medicine in Indiana" program and reception for new residents, which focused on dealing effectively with the stresses of residency training by modifying "Type A" behavior. More than 170 residents and their guests enjoyed this educational and social program at the end of June, which was the culmination of the second year of existence for the RMS.

Again this year, the RMS has concentrated on membership growth. As a result of our efforts, resident representation has increased at both the state and national levels. Our membership increased 175% during 1985 for a total of 203 at the conclusion of year, which will entitle the RMS to four voting delegates at the 1986 ISMA House of Delegates. This is an amazing accomplishment for an organization which had no votes in the ISMA House and no members less than three years ago. On the national level, Indiana resident membership has soared to 441, which is an increase of more than 12% over the previous year. As a result of the boost in AMA participation, Indiana now has five votes at the AMA Resident Physicians Section Meetings and no longer is considered a small state delegation.

The Resident Medical Society has also had a very productive year. In addition to continuing the successful programs established during its first two years of existence, the RMS has produced several new membership benefits for residents since July of 1985. A financial services package and a tax referral service have been among these benefits, as well as a resident physician essay contest in conjunction with INDIANA MEDICINE. A comprehensive insurance package designed especially for resident physicians by American Physicians Life has also been developed and endorsed by the RMS.

Concerns of Indiana resident physicians have also been voiced more often during the past year with the onslaught of budget cuts facing graduate medical education and other significant changes facing medicine in general. Delegates have represented resident opinions and ideals by giving testimony at AMA and ISMA meetings.

In the past year the RMS has also gained recognition from several medical education departments around the state. The Annual "Welcome to the Practice of Medicine in Indiana" program and reception has become a required event for several residency training programs. This included the 1986 "Welcome" program at the end of June which featured J. Pat Tokarz, M.D., of Alexandria, Virginia, discussing coping skills and lifestyle changes to enable residents and their families to manage stress. RMS officers were also warmly welcomed as they traveled around the state for site visits and educational presentations at most of the residency locations. Additionally, some residents were subsidized by their programs to facilitate their attendance at our AMA workshops. This acceptance of the important role organized medicine and its benefits play in the lives of today's physicians in training is a very encouraging sign for the future of organized medicine.

Although the primary goal of the RMS this year was to establish itself as a service organization for residents, it has also provided programs which have been beneficial for other ISMA members and their office staffs. Through co-sponsorship of the AMA "Starting Your Practice" Workshops and the Practice Opportunity Fair, the RMS has served both residents and practicing physicians. In the future I hope the RMS can continue its efforts on mutually beneficial programs, since we can all gain from sharing our perspective and working together to increase participation in organized medicine. As we all know, in these changing times a unified voice representing and supporting all of medicine speaks louder than fragmented or silent ones.

In conclusion, the RMS continues to work on increasing resident membership, expanding services available to residents throughout the state, and making the residency experience and transition into medical practice a positive, rewarding experience.

Personally, it has been a most valuable and rewarding experience to serve the Resident Medical Society, Indiana's resident physicians and organized medicine this past year.

Report of the AMA Delegation

Submitted by: Marvin Priddy, M.D.,
Floor Leader
Referred to: Reference Comm. 6
ACTION: Filed

Before I report on the activities at the AMA Interim and Annual meeting, I want to take this opportunity, on behalf of the AMA Delegation, to thank Dr. Malcolm O. Scamahorn for his dynamic leadership of the Delegation from March 1985 to March 1986.

I am pleased to report that this past year's activity by your AMA Delegation has been both educational and productive. Hopefully this report will prove to be as educational to you and, at the same time, intensify your desire to learn more. If you have any questions about this report, please contact me or one of the other AMA Delegates or Alternate Delegates.

Interim Meeting

The two issues that dominated the reference committees' discussions at the Interim meeting in Washington, D.C., December 8-11, were graduate medical education and medical liability. It was reported that neurosurgeons and obstetricians in Miami and Fort Lauderdale will pay $142,782 for $1.5 million in coverage beginning in January 1986.

The action of the House of Delegates was nearly unanimous in its support of continued funding of graduate medical education. The federal government wants to end financial support under Medicare payments for graduate medical education. The message sent to all our legislators was that financial support of graduate medical education should be continued by all segments of society.

The delegates also voted to support tort reform in those states where there is none, education for the public as to the costs of medical care caused by litigation, associations with other segments of American business being hurt by unfair litigation, and risk management programs for physicians.

There also was considerable discussion about the "Gatekeeper" concept. Every specialty felt they should qualify as a "Gatekeeper." Consequently, no decision could be made and it was proposed that further study by the AMA be made before any final action is taken.

Other actions taken by the House of Delegates included: Strong support and passage of ISMA's resolution in opposition to therapeutic and pharmaceutical substitution; aggressive anti-smoking policy, strong opposition to the continued Medicare fee freeze; a public awareness program emphasizing the physician image; to continue the policy of awarding a state another AMA Delegate for 75% or higher AMA membership; and to join the Massachusetts Medical Society in its suit opposing a new law tying state licensure to Medicare participation.

Annual Meeting

At the Annual meeting in Chicago, June 15-19, Dr. John J. Coury, in his presidential address to the House of Delegates, called on the medical profession to recommit itself to an ethic of viewing the patient as a person. We must not let ourselves be caught up in society's increasing tendency to view individual human beings as "consumers," "beneficiaries" or "recipients." "If people can be reduced to these impersonal terms, it becomes easier to reduce funding of social and health programs," he said. The message he will carry across the nation in his year as president will be that the profession must maintain "its rightful position as a leader in making this nation's health policy," and that "the profession must also become more committed to taking forceful action against physicians who are 'sore spots' in our profession."

Dr. Harrison L. Rogers, Jr. in his last address to the House of Delegates as AMA president, said "we must quit looking back to the good old days and the traditional practice of medicine and unify to protect medicine as a calling, rather than a business. We must realize that medical practice is never again going to be what it was. There is no such thing any more as a best or even better way to practice medicine. We must stop debating issues in terms of traditional versus alternative medical practice because of its alienating affect on both sides of the debate."

Possibly those comments had something to do with the House of Delegates recommendation that the Board of Trustees continue to study a proposal that the AMA sponsor a national health delivery system that could market a health maintenance organization (HMO) or preferred provider organization (PPO), even though a number of delegates urged the Association to go ahead with plans for the new delivery system. A report from the Board to the House said it had decided against it because of "overriding concerns" about conflicts with the AMA mission, adverse internal political ramifications, and financial risk.

The House of Delegates also voted to provide AMA expertise to states where proposals are introduced that would mandate Medicare participation as a condition of licensure in order that physicians in those states may be assured that they will continue to have the option to take assignment on a case-by-case basis; voted strong opposition to any discrimination against any duly licensed and properly practicing physician who is a foreign medical graduate; mandated the AMA work with the government and all third party payors for standardization of mandatory second surgical opinion programs; and adopted a comprehensive program for financing Medicare in the future which includes an IRA for catastrophic illnesses, increasing the eligible age to 67, a "means test," and increased contributions during the work years, all of which I am sure will receive much more discussion and change before Congress will ever accept them.

It was also reported that the AMA is going to continue to help obtain tort reform on a state by state basis because Federal Law could interfere with the state's rights and possibly weaken already in place tort reform; encourage mandatory use of seat belts and shoulder harness for all passengers in automobiles, trucks, and buses; continue to oppose smoking and smoking advertisements and continue to sup-

port antismoking education.

In other actions the AMA endorsed eight "essential elements of quality" as well as a series of guidelines for quality assessment; called for increased physician involvement in efforts to stem the abuse and sexual exploitation of children, including the multimillion dollar child pornography business; approved the establishment of a new Young Physicians Section; rejected the notion that foreign medical graduates (FMGs) who are certified by the Educational Commission for Foreign Medical Graduates (ECFMG) should be eligible to pursue NBMF certification for licensure; called for changes in advertising and labeling of alcoholic beverages to reflect the health hazards of drinking (the AMA Board of Trustees said additional research was needed to determine if alcohol abuse is linked to advertising); endorsed the concept that a medical staff should be independent in exercising medical judgments, although still accountable to the hospital governing body for overall performance; and said children with acquired immune deficiency syndrome (AIDS) and the AIDS related complex (ARC) and children with herpes simplex virus should be allowed to attend school but not preschool.

In addition, the Association announced that it would expand and improve its physician databank so that any hospital medical staff or other appropriate body seeking to verify the credentials and practice history of any physician may receive complete record verification within one week; will pursue federal legislation to raise the federal excise tax on cigarettes and to have those increased revenues apportioned to Medicare; urge Congress to help resolve the current crisis in the price of the DPT vaccine by enacting appropriate tort reform legislation; voted a seat in the House for the American Pediatric Surgical Association, the Renal Physicians Association and the American Academy of Child Psychiatry; voted that physicians under the age of 70 who are fully retired would be eligible for membership at only 20% of regular dues; and will work to reduce the number of deaths due to fire by seeking passage of legislation to require installation of smoke alarms and prepaid response automatic water sprinklers in both residential and non-residential buildings.

In other actions, the AMA House of Delegates agreed to provide information and educational materials to the public and the profession on fraudulent health practices; filed a Council on Ethical and Judicial Affairs report noting that it expects to complete for this year's Interim Meeting its review of conflict of interest guidelines for physicians; endorsed the practice of same-day admission for elective surgery unless the practice is detrimental to the patient's health and agreed to work with appropriate organizations to redefine the beginning and end of a hospital day. They also recommended development of legislation that would require peer review organizations, fiscal intermediaries, insurance companies, and other third parties to accept liability and financial responsibility for injuries to patients resulting from improper review decisions; urged third-party payers to allow for remuneration consistent with services rendered by physicians involved in treating patients at home; and adopted a Medical Student Section resolution that the AMA support medical ethics instruction as a part of the required medical school curriculum.

With all this activity, I am happy to report that the AMA Delegation is staying within its financial budget.

Election Results

It's a pleasure to be able to report that Dr. George Lukemeyer was elected to the Council on Medical Education. Your delegation and the American College of Physicians worked very hard to inform other voting delegates of the fine character and knowledge our Indiana candidate possesses.

A further pleasure to share is the announcement that John A. Knote, M.D. assumed the Presidency of the Organization of State Medical Association Presidents (OSMAP).

In other elections: Dr. William Hotchkiss of Virginia was elected President-Elect; Drs. George Collins of New York, Jack Ring of Illinois, John Tupper of California, and Alan Nelson of Utah were re-elected to the Board of Trustees; and Dr. Ray Gifford of Ohio was elected to fill the one year remaining on Dr. Hotchkiss' term on the Board.

I want to thank the members of the Delegation for their cooperation, hard work, and thorough reporting during the Annual Meeting.

Report of American Physicians Life

Submitted by: Donald Chamberlain, M.D., Chairman of the Board
Referred to: Reference Comm. 4
ACTION: Filed

During 1985, American Physicians Life experienced continued growth, having advanced in terms of product, service support and sales. APL's product portfolio was expanded to include two innovative additions to the company's "Lifestyle Series" of universal life policies. Lifestyle 4 was introduced for those needing moderate amounts of permanent coverage with superior premium flexibility. Lifestyle 5, referred to as "jumbo universal life," was added to the series to provide maximum coverage for physicians ($500,000 or more) at an extremely competitive cost.

Several improvements were made to APL's Professional Disability Income policy to enhance its market appeal including a new lifetime sickness benefit and other benefit enhancements resulting in broader coverage.

Indiana State Medical Association members were also recently introduced to an enhanced association sponsored Group Term Life plan, underwritten and administered by APL. Coverage maximums were increased, benefits improved and costs reduced dramatically.

The ISMA and its members continue to be well represented by Doctor Paul Siebenmorgen of Terre Haute and Doctor Don Chamberlain of South Bend on the APL Board of Directors. Dr. Alvin Haley of Indianapolis actively represents Indiana on the Physicians Investment Company (holding company of APL) Board. These directors are knowledgeable in the operations of the company, and are available to answer questions and provide support as needed for Indiana physicians.

APL's sales division has been strengthened through management team expansion and territorial realignment. In addition, APL began a strong recruiting effort in Indiana to select additional professional agents already serving physicians or currently making their entrance into this upscale market. As a result, sales growth has increased.

APL sales goals for 1985 were achieved. By continuing to provide innovative products and services to meet physicians financial planning needs and recruiting to a select type of agent to represent APL as a specialized life company, APL confidently looks forward to continued growth and progress.

Report of the Physicians Insurance Company of Indiana

Submitted by: Paul Siebenmorgen, M.D., President and Chairman of the Board
Referred to: Reference Comm. 4
ACTION: Filed

Once again, we are hearing the cries of alarm as it relates to medical professional liability insurance. Escalating insurance costs, carriers leaving the market place, carriers changing classifications for some medical specialties, and finally the realization that many physicians have either had to change the way they practice medicine or have quit altogether in order to avoid being sued and paying the high cost of malpractice insurance. You undoubtedly have heard these horror stories and probably have questioned the present status of those who provide coverage and more importantly seek advice as to what's ahead.

With respect to Physicians Insurance Company of Indiana, we are pleased to report that more and more of your colleagues are beginning to recognize the value and advantages of a physician-owned and controlled company. As of May 30, 1986 our policyholder count was up 35% over the same period one year ago. Total premium writings were $1,324,865, which represents an increase of 160% over the same period last year. Our multi-line and commercial insurance programs continue to demonstrate strong gains and as a result are up over 100%. Further, in response to the affordability issue, PICI has developed a premium finance program which allows you two options in paying your malpractice premiums—three installments or monthly. The end result for you is that it allows you to maintain your secure protection plan without creating cash flow problems or diverting funds from your high yielding investments.

In other areas of interest, PICI has developed a marketing plan which includes Dentist's Professional Liability which will be written in conjunction with the office package. We will stress appropriate rate levels as well as conservative reserving posture.

In the areas of claims and claims management, PICI is in the process of strengthening its claims operation so that we can more quickly assist the physician in analyzing and interpreting the factors of medical incidents. We believe that the compiling of pertinent documentation, evaluating the merit of the medical incidents, and finally formulating a strategy for the most cost efficient defense and resolution are critical and essential steps to effective claims management. We will continue to fight frivolous and unwarranted claims with the utmost rigor by the continued utilization of the top defense attorneys in the state.

This report would not be complete without acknowledging Dr. Martin J. O'Neill for his outstanding leadership and guidance as the first President and Chairman of the Board of Physicians Insurance Company of Indiana. It is under his leadership that your company has grown and prospered.

Finally, I believe that we are in much

Report of the Physicians Insurance Company of Indiana

better shape than our colleagues in other states because of the wisdom of our legislators, the ISMA and other parties with the enactment of the Indiana Medical Malpractice Law. As we look around, other states' frequency and severity continue to escalate, effective tort reform packages are not passed, occurrence form of reinsurance is almost non-existent—all of which are having negative impact on rates nationwide. We can take solace in the fact that our rates have remained fairly constant since the inception of our company. However, we cannot allow ourselves to be lulled into a false sense of security. We will continue to emphasize rate and reserving adequacy and fiscal stability so that we can continue to provide you with the finest in claims and policyholder services available. With your continued support and the resources of the Indiana State Medical Association, we will continue to be that source of security.

Annual Reports of Commissions

ACTION: All reports filed.
(Commission members are listed in the October 1986 issue of INDIANA MEDICINE, page 895.)

Physician Impairment

Submitted by: Larry M. Davis, M.D.
Chairman
Referred to: Reference Comm. 5

The Commission's focus in recent years on developing "The Indiana Network for the Impaired Physician" continued with individual commissioners being active in assisting the formation of hospital and county medical society impaired physician committees, in the production of our third annual Spring Training Seminar for those working in Indiana with impaired physicians, and in our ongoing efforts to increase awareness about physician impairment both within and outside the medical community. In late 1985 on the occasion of the ISMA Annual Meeting, the commission felt honored to have been principally responsible for the scientific session with Doug Talbott, M.D. and Nancy Roeske, M.D. joining commission members for an afternoon's presentation on impaired physician issues. On behalf of the ISMA commission, I attended the annual American Medical Association Convention in the Spring of 1986 in Chicago and brought back specific information which proved useful to the progress and development of the ISMA Commission. Funding issues and strategies for increased funding were discussed and a new developing organization of Chairmen of Impaired Physician activities in the various states was initiated. Also, at both the AMA meeting and the ISMA Spring Training Seminar a few weeks later, issues concerning relationships with medical licensing boards, and the Indiana Licensing Board in particular, were presented and discussed. Although progress has been made, much more effort must be extended to develop an ongoing and workable relationship with the Medical Licensing Board that accomplishes the purposes of both organizations to protect the consumer and to manage and rehabilitate when possible the competent physician rendered ineffective by treatable impairments.

Cases of impaired physicians in various parts of the state continue to surface only after the impairment has progressed to a marginally treatable level. The ISMA Commission on Physician Impairment will continue to push for improved identification and management of impaired physicians. We anticipate new challenges in the future, to meet the needs of the number of physicians succumbing to the increased stresses of today's medical practice.

Public Relations

Submitted by: Adrian R. Lanning, M.D.,
Chairman
Referred to: Reference Comm. 5

The 1985 House of Delegates issued a new challenge to the members of the Commission on Public Relations when it voted to support three public policy proposals—the tobacco-free society by the year 2000, a mandatory helmet law for motorcyclists, and the reduction of the blood alcohol content required for a drunk driving conviction from .10 percent to .05 percent.

These issues were presented as legislative initiatives, but in order to bring them to the attention of the Indiana General Assembly and garner support, it was determined a public awareness campaign was necessary.

The public relations and legislative staffs collaborated on all three issues. The status of each follows:

Tobacco-Free Society by the Year 2000

The resolutions concerning tobacco that will be presented at this convention reflect several months of activity by ISMA. During that time ISMA was instrumental in forming the Indiana Coalition for a Tobacco-Free Society. The Coalition includes the American Cancer Society, the Indiana Heart Association, the American Lung Association of Central Indiana, the Indiana State Board of Health, the Indiana Academy of Family Practice, the Indiana Association of Osteopathic Physicians, the Indiana Dental Association, the Marion County Health and Hospital Corporation, the Indianapolis Heart Institute, the Indiana Public Health Association, and the Marion County Medical Society.

The coalition's effort as it relates to public awareness will be kicked off during the 1986 ISMA Annual Meeting and will coordinate with the American Cancer Society's Great American

Smoke Out in November. New conferences, public service announcements, and news releases will be used to draw attention to our efforts. Perhaps one of the most gratifying developments in this campaign has been the response of ISMA members to a request that they participate by agreeing to talk to their local media about tobacco and health. When the call went out through ISMA REPORTS for these "Media Docs," numerous physicians answered, many of whom voiced their tremendous concern about the health hazards of tobacco. It is obvious that we have tapped a "nerve" within our own membership about this single most preventable cause of death in our time.

Concurrent with the convening of the Indiana General Assembly in January, ISMA and the Coalition are planning a media event, the Great Indiana Tobacco Pitch, an event scheduled to draw public and legislative attention to our efforts.

Legislatively, ISMA will work to gain passage in the General Assembly of bills that would restrict/ban smoking in government buildings, prohibit the distribution of free samples of cigarettes and other tobacco products and raise the minimum age for tobacco sales. Each of these bills will be considered in resolution form by the 1986 ISMA House of Delegates.

Another focus of the public awareness program is on children. Studies show that boys in the third and fourth grades are already beginning to try cigarettes and tobacco products. Over the next few months, various ISMA members in the state will be available to their local schools to talk about the hazards of smoking and tobacco use. The success of each of the components of this tobacco free society initiative rests with all of us as we continue to work for this important goal.

Motorcycle Safety

Much of this past summer has been spent in collecting data on motorcycle accidents. ISMA's legislative and public relations' staffs met with representatives from the Indiana State Police, the Indiana Department of Highways Traffic Safety Division, the Indiana Department of Education, the Insurance Institute, the Indiana Osteopathic Association and the Indiana Hospital Association to determine the availability of information to be used in drafting legislation. The group recommended that ISMA expand its goal of reinstating the motorcycle helmet law to working toward increased motorcycle safety education.

The Indiana State Police, at ISMA's request, agreed to begin to note on motorcycle accident reports whether the motorcyclist was wearing a helmet. Much of the information gathered will be used in news releases and radio feeds promoting motorcycle safety.

Drunk Driving

ISMA agreed to co-sponsor a Drunk Driving Awareness Program along with the Sports Car Club of America, the Indiana State Police, and MADD. The program was designed to test driver ability, reaction time and attitudes after the participants consumed enough alcohol to test .05 percent, .08 percent, and finally, .10 percent blood alcohol. ISMA's public relations department promoted the event, which was held in Indianapolis, July 12, through news releases and public service announcements. The event drew coverage from three Indianapolis television stations, Network Indiana, which includes radio stations all over Indiana, and three Indianapolis radio stations. It was obvious after comparing the "control" drivers' scores with those who drove after consuming alcoholic beverages that significant impairment occurs at each level.

'Healthy, Happy and Wise'

A year ago, ISMA targeted senior adults, a group with whom physicians share many common interests and concerns, for a public education video series called "Healthy, Happy and Wise." An update is in order. The six half-hour television programs were rebroadcast on various PBS stations this summer and fall. In the first six months of this year, ISMA has made tapes of the program available to more than 50 senior citizen centers, retirement homes, clinics, and senior church groups. Most of the groups viewed the entire series. Six sets of the videotaped series have been purchased by county medical socities, physicians, hospitals, or clinics to be used for local programming.

In May, "Healthy, Happy and Wise" received the Bronze Quill Award from the Fort Wayne Chapter of the International Association of Business Communicators. A 1985 public opinion poll on physician image noted that people of retirement age have high opinions of doctors. "Healthy, Happy and Wise" has been an excellent vehicle for solidifying those opinions.

Continuing Programs

In other external public relations efforts, the ISMA conducted the Physicians Community Service and Journalism Awards competition once again this year.

Turning to internal public relations efforts, the staff conducted a Spokesperson Training Seminar for ISMA leaders, which included videotaped interviews of the participants. In addition, the public relations department is developing a list of physicians who can be media spokespersons in their specialty and in their locale. This will allow ISMA to respond more quickly to media requests for health and medical information.

ISMA publications, INDIANA MEDICINE, ISMA REPORTS, MACS FACTS and the PRoFile, continue to inform the members about medical issues and ISMA activities.

"Your Hoosier Doctor Says," the ISMA's weekly newspaper column on health and medical topics, was carried in more than 60 newspapers. Between January and June, ISMA's public relations department received 68 calls from newspapers or radio and television news departments. Many of the requests resulted from our news releases, or from articles in our "Hoosier Doctor" columns.

I would like to thank the members of the Commission on Public Relations and the Public Relations staff for their continued hard work on behalf of the Indiana State Medical Association.

Medical Education

Submitted by: Franklin A. Bryan, M.D., Chairman
Referred to: Reference Comm. 4

The ISMA Commission on Medical Education and its Subcommission on Accreditation met on November 3, 1985 and March 23, 1986. Shokri Radpour, M.D. was named Vice Chairman of the Commission. Eugene Gillum, M.D. chaired the Subcommission and Kelly Chambers, M.D. was appointed the Vice Chairman of the Subcommission.

The major activity of the Commission and Subcommission has again been that of accreditation/reaccreditation of institutions and organizations for providing intrastate continuing medical education. During the year there were four institutions and two organizations reaccredited for providing intrastate continuing medical education. There was one organization granted initial accreditation. In total, there were seven accreditation/reaccreditation actions this year. There were no actions either deferring or denying accreditation.

In preparation for the site visit by the Committee for Review and Recognition (CRR) of the Accreditation Council for Medical Education (ACCME) several modifications were made in the ISMA accreditation/reaccreditation process. First, the Commission upon the recommendation of its Subcommission granted an initial accreditation to the ISMA Section on Directors of Medical Education and the Association of Indiana Directors of Medical Education. These bodies through the action of the CME Committee of AIDME will now serve as the joint sponsors for the ISMA and its sections, commissions and committees to provide CME.

A second action consisted of preparing and approving a specific appeals process to be followed in case of an adverse decision recommended by the Subcommission on Accreditation with acceptance by the Commission.

The third was in the preparation and acceptance of a procedure manual to assist the institutions and/or organizations, the subcommission members, commission members and the site visitors in the accreditation/reaccreditation process.

Another action related to the accreditation/reaccreditation process is the requirement that each institution accredited or reaccredited after January, 1986 shall submit an annual report to the Subcommission/Commission prior to March 31st of each year. Continued accreditation shall be contingent upon receipt and approval of said annual report.

The ISMA was again honored by the ACCME which requested Mrs. Beckett Shady-King to do a site visit for them on January 28, 1986. This site visit was at the Iowa State Medical Society.

On October 10, 1985, Mrs. Shady-King and Dr. Bryan attended the Annual ACCME/State Medical Society Invitational Conference on CME held in Chicago. Dr. Bryan participated in a debate on the "Effectiveness of the CME Essentials within the State." He spoke on the "con" side of the present ACCME Essentials. This debate surely made the representatives of 40 states and the ACCME think.

Dr. Bryan, as a member, attended the CRR meeting in Chicago on October 31, 1985. The applications of ten state medical societies were reviewed and actions were taken on the recognition of them as accreditors of institutions and organizations for providing intrastate CME. Following this meeting, Dr. Bryan attended the ACCME meeting on November 1, 1985 as a guest.

At the meetings of the Subcommission on Accreditation and the Commission on Medical Education on March 23, 1986, the ISMA was reviewed by a site visit team from the CRR of the ACCME. The team's report was favorable; however, action upon it by the CRR will take place in October, 1986. Recognition is expected since our program does meet the criteria for recognition. The only concern expressed by the site visit team was related to the continuity of administration of the ISMA's accreditation program. This was in reference to ISMA staff and chairmen of the Commission and its Subcommission.

The chairman wishes to express his appreciation to the Commission Vice Chairman, Dr. Radpour, the Subcommission Chairman, Dr. Gillum, and its Vice Chairman, Dr. Chambers, all of whom contributed so much to the ISMA program. The members of both bodies and the site visitors also contributed much to the success of the program and their services are likewise greatly appreciated.

A special tribute and thanks are given to the ISMA staff whose activities on the state level have assured the Commission's success. Mrs. Beckett Shady-King is largely responsible for this. In addition, we are honored by her activity at the national level as a site surveyor for the ACCME for other state medical associations'/societies' CME accreditation programs. Without her the ISMA could not be considered either for recognition as an accrediting body or as a source for consultation and review of other state societies.

Sports Medicine

Submitted by: Ronald G. Blankenbaker, M.D., Chairman
Referred to: Reference Comm. 4

Over the past several years the primary objective of the Commission on Sports Medicine has been to encourage good health and physical fitness in our Hoosier youth through safe, effective sports activities in school and amateur athletic programs. Since the last annual report, the Commission has met on a bi-monthly basis with various additional subcommission endeavors to meet this objective.

The first priority of the Commission was the planning of statewide seminars designed to assist team physicians, trainers and school officials in their efforts to provide a safe environment for competitive sports. The first of these seminars will be held in Lake County in October, 1986. Other seminars are planned in the future for representative areas throughout the state. Furthermore, the commission has developed programs and efforts to encourage every school corporation to ob-

tain a sports physician and to provide qualified trainers or similarly qualified individuals to support this physician. Much of these activities were stimulated by a study of athletic health care management in Indiana's secondary schools by the Governor's Council on Physical Fitness and Sports Medicine and reported in the December issue of INDIANA MEDICINE.

As a further outcome of these endeavors the commission is working with the Governor's Council on Physical Fitness and Sports Medicine and the Indiana Athletic Trainer's Association to develop legislation that will initiate and fund a faculty/athletic trainer program for Indiana. This program would train designated faculty members during the summer to ultimately become fully qualified trainers for their respective schools. This would allow us to overcome a significant deficit in our state over a five-year period after which essentially every school would have a qualified trainer on-site. Funding will be a key issue to successful legislation and support from the Indiana Department of Education will be essential.

In a related matter the Commission has been evaluating a concern that officials (referees, etc.) have become lax in their reaction to high risk situations, i.e., spearing in football, etc. We have met with many of these officials, especially for football and basketball, in conjunction with the Indiana High School Athletic Association (IHSAA). It is our hope that these officials will become more acquainted with our sports medicine activities and better utilize the team physician in a competition situation.

Most of these efforts will not only improve the quality of care for athletes, but will also resolve much of the injury reporting problem we have recognized over the past several years. The better the quality of care, the more reliable is the reporting of injuries, and with better reporting comes more useful data for the development of effective programs.

The commission has been wrestling with the need to develop some form of roster of qualified sports medicine physicians who are available to support the ever increasing number of national and world-class amateur athletic events in our state. While ISMA is not a credentialing organization, the commission determined (and the Board of Trustees agreed) that it would be appropriate to survey all members of ISMA regarding their training, experience and interest in amateur athletic activities. The results of this survey will be kept confidential (for ISMA use only) and will be updated on a regular basis. This will allow for the most efficient use of our physician resources throughout the state and provide assurance that this information will not be abused. The first such survey should be mailed to members sometime in October.

The Commission has been regularly kept up-to-date on the medical services developments for the Pan American Games to be held in Indiana next August and, as such, has served an important advisory role. Additionally, ISMA is well represented on the Medical Advisory Committee of the Medical Services Division of the local Pan Am organization and many commission members have key roles in that division's activities. Consequently, ISMA is playing a very important role in the planning and implementation of the Games — we hope that the general membership will become actively involved in this event over the next year.

The commission continues to evaluate specific issues related to sports medicine and to develop position papers where appropriate. The school physical exam form developed by the commission has been presented to all Indiana high schools and many are now using it. Similarly, a position paper on the means of safely losing weight for wrestling events has been disseminated to all schools. The commission is currently evaluating: The safety of boxing, the uses of anabolic steroids and other drugs in high schools, recommendations for safer equestrian events, the use and abuse of splints and braces, and the controversy surrounding when an athlete should return to competition following a head and/or neck injury. Reports will be forthcoming on many of these issues.

The commission is in the final stages of planning for a major statewide sports medicine event to be held in September at the Governor's residence. We are co-sponsors with the Governor's Council on Physical Fitness and Sports Medicine and will invite representatives from sports and fitness-related organizations from throughout the state. The purpose of this reception is to create a social interchange and a better awareness of what is happening in sports and medicine and physical fitness programs in Indiana. Furthermore, it is our hope that stronger, lasting relationships will develop from this meeting that will reap very positive benefits in the future.

It has been a busy year and much work is yet to be done. We would like to thank the members of the Commission and its Technical Advisory Subcommittee for their dedicated efforts. The fruits of their work is obvious and will be evident in sports activities for many years to come.

Medical Services

Submitted by: Michael O. Mellinger, M.D., Chairman
Referred to: Reference Comm. 4

The business of the ISMA Commission on Medical Services involves actions mandated by the ISMA House of Delegates as well as interim issues referred by the ISMA Board of Trustees.

As promised in last year's annual report, a committee consisting of both ISMA members and representatives of the Indiana Association of Pathologists has met repeatedly during the past year to formulate statewide transfusion guidelines. I am pleased to report that the work of the committee is now completed and the guidelines have been published in INDIANA MEDICINE. Special recognition should be given to Leonard Boral, M.D., for his diligent efforts in bringing this project to fruition.

In response to Resolution 85-3A, the Commission on Medical Services spent

considerable time trying to find a legal way for ISMA to negotiate with third party payors. Unfortunately, collective bargaining is unlawful for the vast majority of Indiana's physicians. We did, however, explore the concept of having two particularly adept CPA firms represent the interests of individual physicians. At the time this report is being written, the Board of Trustees has given conceptual approval of this concept and we anticipate that you will be receiving specific information in the mail.

In response to Resolution 85-13, the Commission on Medical Services is in strong agreement that physicians should be included on hospital boards of directors. To that end, we have asked the Commission on Legislation to seek a sponsor for appropriate legislation in the Indiana General Assembly.

In response to Resolution 85-27, the commission has developed a package of business services to be made available to ISMA members. The package includes discount purchase arrangements, special banking programs, discount stock transactions, as well as specially designed insurance programs. All of the programs have been designed to provide you with a financial advantage. At the time this report is being written, the Board of Trustees has given the Commission conceptual approval while the specific details are still being resolved. I anticipate that all ISMA members will be receiving information directly regarding these programs.

I would like to thank the members of the Commission who gave generously of their time and efforts.

Subcommission on Insurance

Submitted by: Michael O. Mellinger, M.D., Chairman
Referred to: Reference Comm. 4

The Subcommission on Insurance continues to be very involved in monitoring the ISMA member's group health insurance program. This program is operated on a cost-plus basis with Lincoln National Life being hired to perform part of the administrative functions. As the Subcommission received feedback from you, the participants in the plans, we continue to refine the rates and benefits structure.

I am pleased to report that, once again, we are not anticipating any increases in premiums. ISMA now offers five health insurance plans with varying combinations of deductibles and cost containment features. With more than 4,000 participants in the plan, the plan has become both stable and reasonably predictable.

I would like to personally thank the members of the subcommission for the diligent attention they have given to the complex topic.

Legislation

Submitted by: Edward L. Langston, M.D., Chairman
Referred to: Reference Comm. 3

1986 has been a busy year for the members of the Commission on Legislation as well as the recently created Department of Government Relations. Even though the 1986 session of the Indiana General Assembly was a "short" session in days, it was not short in the volume of legislation affecting the practice of medicine in Indiana.

At the request of ISMA and in accordance with Resolutions adopted by the 1985 House of Delegates, several legislative proposals were introduced for consideration: the Uniform Determination of Death Act, mandatory motorcycle helmets, lowering the blood alcohol content to .05% for drunk driving, allowing more than one lab to conduct tests on infants to detect inborn errors of metabolism, and requiring physicians on publicly-funded hospital boards.

The ISMA was successful in the passage of the Uniform Determination of Death Act which places in the Indiana law the medically accepted definition of brain death as well as the common law definition of death. This measure was adopted by the AMA and the ABA. Indiana now joins the majority of states with a Uniform Determination of Death Statute.

Two "drug-related" proposals were introduced in the 1986 Session and were defeated with the support of the ISMA. The first proposal would have restricted the ability of physicians to dispense medications from the office. The second proposal would have established a "triplicate prescription" program under the auspices of the State Police. It is likely that we will see both of these proposals return to the legislature in 1987 for consideration in some form.

In accordance with a Resolution adopted by the AMA and the ISMA's House of Delegates, our lobbyists testified in favor of a measure in the Indiana House which would have restricted smoking in government buildings to designated smoking areas. This bill lost by a narrow margin on third reading. The ISMA will continue to fight to move Indiana towards a Tobacco-Free Society by 2000. A coalition of nearly 20 health care organizations in Indiana including the ISMA has been formed to carry out a three-part proposal, one being the adoption of legislation designed to lower the use of tobacco especially by minors. The ISMA will be actively supporting these legislative measures in the 1987 session.

A legislative proposal to establish an "allied health screening panel" was defeated in the 1986 session. In addition, the ISMA was instrumental in the defeat of several legislative measures to include perfusionists under the Indiana Medical Malpractice Act.

The issue of mandatory screening of hospital patients and pre-marital applicants for the presence of the HTLV-III antibody was defeated in the Indiana General Assembly. A similar proposal likely will be reintroduced in the 1987 Session. Indiana also now has a new law that should help families better understand the procedures for organ and tissue donations.

To help summarize the new state laws that affect the practice of medicine, the Government Relations Department published a "Digest of Health and Medical Laws of the 1986 Indiana General Assembly" as well as

a 1986 supplement to the "Physicians Guide to Indiana Law" for the membership of ISMA. In addition, the Commission on Legislation has been asked to review and comment on proposed state rules that concern the practice of medicine in Indiana.

The leadership of the ISMA and the members of the Commission on Legislation also have been kept apprised of federal legislative proposals and key votes—especially related to changes in the Medicare Program—so that our lawmakers in Washington can hear directly from the members of the ISMA on these key proposals.

Throughout the summer, several ISMA physicians shared their concerns on health/medically related legislative proposals with members of the Indiana General Assembly and state legislative candidates. These dinners helped to increase the ISMA's legislative efforts by providing a forum where legislators and physicians can meet one-on-one and discuss these important issues.

The ISMA's key contact program, which is an extremely important "grass-roots lobbying" tool, has grown in membership. The goal is to have at least one ISMA member "key contact" for each state legislator. The ISMA Auxiliary has been very helpful in many of these legislative efforts at the local, state, and federal level.

As we look to the next session of the Indiana General Assembly, the ISMA's administrative support has undergone some changes. Richard King, who has been a tremendous asset to the ISMA's legislative efforts, is now the Executive Director of ISMA. One of his legislative assistants, Julie Newland, is now the Director of Government Relations. Ronald Dyer is now ISMA's General Counsel. Greg Bowes left the Legislative Department and now is enrolled at the Georgetown Law School's International Center.

I would like to thank Rick, Julie, Ron, and Greg for their able assistance and would also like to extend my appreciation to all of the members of the Commission on Legislation, the auxilians, the key contact physicians, and all of the other ISMA members who take time out of their busy schedules to share with the lawmakers their ideas to help to ensure that Indiana is a good place to practice medicine and that our citizens receive quality health care.

Constitution & Bylaws

Submitted by: Lloyd L. Hill, M.D., Chairman

Referred to: Reference Comm. 2

During the year the Commission on Constitution and Bylaws had several resolutions submitted to it for implementation into the ISMA Constitution and Bylaws.

Among other things the Commission on Constitution and Bylaws considered the following:

1. Who should be allowed to submit resolutions to the House of Delegates
2. Pursuant to Resolution 85-2, made appropriate recommendations to the Board of Trustees to provide for membership of active-duty military physicians
3. Pursuant to Resolution 85-23, made appropriate changes in the Bylaws pertaining to the Hospital Medical Staff Section
4. Pursuant to Resolution 85-24, made changes to the ISMA Constitution to be in compliance with recent changes to the Bylaws
5. Pursuant to Resolution 85-25, the Commission implemented the resolution dealing with Resident Medical Society representation on the ISMA Board of Trustees and the ISMA House of Delegates.

Your Commission Chairman wishes to thank the ISMA staff and members of the commission for their assistance during this past year.

ACTION: All reports filed except where noted otherwise

(Committee members are listed in the October 1986 issue of INDIANA MEDICINE, page 896.)

Medico-Legal

Submitted by: John W. Beeler, M.D., Chairman
Referred to: Reference Comm. 3

The Medico-Legal Committee met during 1986 and among other things reviewed revisions to the "Medical-Legal Compact of Conduct of the Indiana State Bar Association and the Indiana State Medical Association" and have recommended the approval of same by the ISMA House of Delegates after approval of the ISMA Board of Trustees.

In addition your Committee continued to monitor the filing of nuisance suits and lawsuits involving multiple defendants without good cause. The Medico-Legal Committee has prepared a resolution addressing itself to multiple defendant litigation and will continue to monitor and make recommendations as appropriate.

The Committee continues to monitor the filing of lawsuits of less than $15,000.00 and will continue to closely monitor the situation.

As chairman I wish to thank the other members of the committee who assisted with the work of this committee throughout the year.

Medical Education Fund

Submitted by: John W. Beeler, M.D., Chairman
Referred to: Reference Comm. 4

The Indiana Medical Education Fund received $62,138.35 that was provided by the Auxiliary fund-raising activities and physicians' contributions. Previous contributions have been $57,179.20 for 1985, $68,244.35 for 1984, $66,489.88 for 1983, $59,372.97 for 1982, and $55,556.83 for 1981.

The Medical Education Fund Committee met on March 19, 1986. The investment portfolio performance was reviewed for the prior period and a total return of 10.2% was reported for the period of 7/1/84 to 3/17/86. The future anticipated performance of the fund was also reviewed. The American Fletcher National Bank's trust department representatives were very positive about the fund's future growth.

Fund Balance 7/1/85	$620,565.56
Contribution	62,138.35
Net Investment Income	43,650.10
Trustee Fees	(2,456.69)
Disbursement to IUSM	(60,000.00)
Ending Balance 6/30/86	$663,897.32

Grievance

Submitted by: G. Beach Gattman, M.D., Chairman
Referred to: Reference Comm. 5

The Grievance Committee continued to work on complaints against physicians during 1986.

As usual the lack of good patient communication is the reason for most of the complaints that have been received. As chairman, I wish to thank the other members of the committee for their willingness to serve during the year.

Future Planning

Submitted by: William C. VanNess II, M.D., Chairman
Referred to: Reference Comm. 5

The Future Planning Committee has again had a busy year. In response to Resolution 85-26, the Future Planning Committee has taken the related issues of field staff representation and ISMA organizational structure and has recommended to the Board of Trustees that ISMA become actively involved in a total strategic planning process. To that end, the Future Planning Committee is currently conducting a series of meetings, both at the ISMA headquarters as well as other locations throughout the state, in an attempt to identify physician needs throughout the state and then develop definitive plans to meet those needs. The objective of this activity will be to assure that ISMA's physical facilities, staffing complement, activities and budget are all appropriately geared to meeting the needs of the dues-paying member.

We have also continued to struggle with ISMA's building needs. During the past year, we have continued to explore building options and have made appropriate recommendations to the Board of Trustees.

While no definitive actions have been taken during the past year, the Future Planning Committee continues to monitor the issue of fee review as well as the issue of physician supply and distribution within the state.

I would like to thank my committee members for a job well done. The committee members have spent many hours in meetings and on the road and I would like to extend my appreciation for all their efforts.

Negotiations

Submitted by: John A. Knote, M.D., Chairman
Referred to: Reference Comm. 5

The Negotiations Committee did not meet in 1985-1986 as there were no requests for assistance in this area. Future directions, it would seem on the basis of discussion with several officers and other members, may well take the form of a clearinghouse for negotiations assistance to those groups or individuals in need of that service. The reorientation of our efforts would be well served by continued participation of those who have had previous negotiations seminar instruction at the AMA level and who retain an active interest in this area, in order to assist in those situations where negotiations are necessary in the future.

Reduce Drunk Driving

Submitted by: Michael B. DuBois, M.D., Chairman
Referred to: Reference Comm. 5

The Reduce Drunk Driving Committee focused its attention in 1986 towards efforts to change Indiana's statute to lower the per se illegal blood alcohol level (BAC) from .10% to .05%.

To this end, a resolution was adopted by the ISMA 1985 House of Delegates supporting such a measure. A bill was introduced in the 1986 session of the Indiana General Assembly which unfortunately failed to receive consideration by the lawmakers. The Reduce Drunk Driving Committee will continue to work with the Governor's Task Force and the ISMA Commission on Legislation to urge consistent application of the current drunk driving laws throughout the state.

The Reduce Drunk Driving Committee also recommended to the ISMA Executive Committee and the Board of Trustees that the ISMA and its county medical societies support the 1988 Hoosiers Against Drunk Driving (HADD) Conference designed to educate the young driver about the dangers of drinking and driving.

Other activities of the Reduce Drunk Driving Committee include guidelines for model alcohol abuse evaluation and treatment; continued support of the activities of the Governor's Task Force to Reduce Drunk Driving; endorsement of Indiana's safety belt law; and research into national efforts directed towards intoxicated boat operators.

The Reduce Drunk Driving Committee would suggest that when a resolution has been approved by the ISMA House of Delegates that at least the chairman (if not the entire membership) of the commission or committee that sponsored the resolution be invited to all meetings of the commission or committee to which said resolution has been referred for implementation.

I wish to thank all of the members of this committee for their continued support and hard work in helping to make Indiana's citizens more aware of the dangers of drinking and driving so as to make our roads safer. The committee looks forward to working with other interested groups to establish consistent application and enforcement of our drunk driving laws.

Ad Hoc Medical Malpractice Advisory Committee

Submitted by: J. William Wright Jr., M.D., Chairman
Referred to: Reference Comm. 3

ACTION: Referred to the Board of Trustees for re-evaluation of the future role of this ad hoc committee

The ad hoc Committee on Medical Malpractice did not meet during this past year. The committee gave the ISMA staff the monitoring responsibility during the interim.

In that regard several issues have been addressed by the ISMA leadership and Legislative Commission such as the increase in the Patients' Compensation Fund (PCF) surcharge, structured settlements, and the overall viability of the PCF.

Our representatives have attended several administrative hearings regarding issues affecting Indiana's Medical Malpractice Act and the professional liability coverage such as Territorial Rates.

The ISMA took a leadership role in arranging for several meetings with the Insurance Commissioner of Indiana, legal counsel, and numerous interested parties regarding the Patients' Compensation Fund and prospects for the 1987 Legislative session.

Ad Hoc Committee on I-PRO

Submitted by: William H. Beeson, M.D., Chairman
Referred to: Reference Comm. 5

When DRGs and corresponding mandated peer review were legislated by the federal government, the Indiana State Medical Association played an active role in encouraging the formation of a physician based peer review organization. This was done in the spirit that physicians themselves could best assess the quality and appropriateness of their actions and that physicians were in the best position to guard against the possibility of mandated cost reductions in medical care resulting in inferior quality of medical care for our aging patients.

While the organization of such a peer review committee was felt best to be done at an arm's length relationship with the Indiana State Medical Association, a close monitoring of such an organization and strong lines of communication should be established and maintained. To this end, President Larry Allen appointed an Ad Hoc Committee of ISMA Trustees to perform this function. Dr. Paul Siebenmorgen, ISMA President, agreed with this philosophy and reappointed this Ad Hoc Committee to function during his current tenure as ISMA President.

During the past twelve months your ad hoc committee has been actively involved in carrying out its prescribed functions. Following the 1985 ISMA Convention in South Bend, the committee had the opportunity to meet with members of the I-PRO Board. At that meeting, discussions were held on numerous topics including:

1. Disciplinary action regarding physicians with excessive number of denial admissions.
2. Regional instruction seminars to instruct physicians on ways to more effectively and efficiently deal with the current peer review system and on future anticipated changes in the peer review process.
3. Periodic meetings between the I-PRO leadership and the ISMA Ad Hoc Committee regarding I-PRO.

During that post-convention meeting and in the following months of 1985, the Ad Hoc ISMA Committee proposed that a workshop or seminar be organized and provided at regular intervals to assist physicians with excessive numbers of denials on how to better comply with IPRO and HHS regulations and policies and how to work within the guidelines of the presently established system. It was felt that this would be a voluntary service available to physicians and one which would be most important for physicians who were under disciplinary action from the federal government regarding excessive numbers of denied admissions. It was also proposed that regional instructional seminars to instruct physicians on dealing with the current peer review system and on anticipated future changes be conducted at nine regional centers throughout the state. It was felt that this would allow physi-

cians from all areas of the state to be within approximately one hour's driving time from such meetings and thus facilitate attendance. It was proposed that these meetings be jointly sponsored by the ISMA and by I-PRO. It was felt that each program would be educational in nature and that every attempt would be made to avoid allowing such seminars to degenerate into an emotional debate of the DRG system. In addition, it was felt that these meetings would allow an opportunity for the I-PRO Committee to make the I-PRO leadership aware of complaints from ISMA members which had been addressed to the Ad Hoc Committee. It was also suggested that I-PRO provide regular contributions to INDIANA MEDICINE which would be educational in nature and which would supply support information similar to the information proposed by the aforenoted educational seminars.

On January 21, 1986, the Ad Hoc I-PRO Committee met with representatives from I-PRO in an extremely productive and candid meeting. Discussions were held regarding the formation of the financial structure of I-PRO and rumors that I-PRO was going to change to a for-profit corporation. The ISMA Ad Hoc Committee emphasized to the I-PRO administrative officials present that:

1. It would be extremely important to conduct the proposed educational seminars early in 1986 in order to provide effective and timely "education" for ISMA physicians prior to proposed changes in the review process enforcement.
2. That the Ad Hoc Committee would be extremely concerned if I-PRO did not have an annual meeting in order to enable its 1,800 physician members to vote for its board of directors and to have an opportunity to vote on any change from a not-for-profit to a for-profit status.

In subsequent weeks and months, numerous communications and meetings were held between various ad hoc committee members and the I-PRO leadership and administration.

Many recent developments have occurred regarding DRGs and I-PRO. In approximately March of 1986, hospitals were no longer awarded waiver of denials. This resulted in hospitals, as well as physicians, no longer receiving reimbursement for denied admissions. It is anticipated that this will have a significant financial impact on many hospitals and physicians. In addition, quality has become a criteria for which denial of admission can be made. If it is felt that an inferior quality of care has been delivered to a patient, I-PRO can deny the admission and subsequent payment to both physician and hospital. In addition, the patient is notified that this denial was due to perceived inferior quality of health care delivered. Both I-PRO and the ad hoc committee are extremely concerned that such communication will lead to litigation and a breakdown of the physician-patient relationship. However, this is a federally mandated notification.

In May of 1986, it was learned that I-PRO was in the process of changing to a for-profit corporation. An offer was made to the Indiana State Medical Association Board of Trustees regarding possible purchase of approximately one-third of corporate stock in this newly formed corporation. The Board of Trustees actively discussed this possibility and voted negatively on such purchase. At a subsequent board meeting, it was felt that the possibility of future purchase of I-PRO stock (in the for-profit corporation) should be discussed and voted on by the ISMA House of Delegates at the upcoming October Convention.

It has been hoped that the educational seminars could be held early in 1986 regarding proposed peer review changes and implementation of new regulations. However, logistical and administrative problems at I-PRO did not allow such seminars to be held until June of 1986. Thus far two such seminars have been held—the first in Indianapolis, and a second in Muncie. It is anticipated that additional seminars will be held in various areas of the state in the Fall of 1986. Recent issues of INDIANA MEDICINE have contained articles from I-PRO which have been of an informative and educational nature. It is anticipated that these will continue and that they will be of significant informational benefit to ISMA members.

I would like to thank the other members of the ISMA Ad Hoc I-PRO Committee for their time and contributions, as well as the members of the I-PRO board and administrative staff for their time and cooperation. As a special note, I would like to thank Co-Chairman Dr. John Luce for his significant contribution and guidance. Personal reasons necessitated Dr. Luce's resignation from both the Board of Trustees and the Ad Hoc Committee earlier this year. However, Dr. Luce has continued to be an extremely valuable resource for the Ad Hoc Committee and we are all extremely indebted to him for his assistance and dedication.

Ad Hoc Study Committee on AIDS

Submitted by: Lawrence E. Allen, M.D., Chairman
Referred to: Reference Comm. 5

The Indiana State Medical Association Ad Hoc Study Committee on AIDS met with members of the Indiana State Board of Health to discuss this onerous problem.

The Indiana statistics regarding AIDS as of April 30, 1986 indicated there were 83 cases of AIDS in Indiana and 45 deaths had been attributed to AIDS as of that date.

The number of AIDS cases doubles in each 9-12 month period. With this ratio, Indiana would expect 2,000-3,000 cases of AIDS by the end of 1990. It is important to treat AIDS early. If an AIDS patient's life can be prolonged for even one year, the possibility for new treatment is evident. 3%-6% of HTLV-III positive convert to AIDS annually.

The committee was apprised that the Indiana State Board of Health has received numerous calls from physicians stating that the physician did not list the cause of death on the death certificate as AIDS due to pressure from and respect to the victim's family.

The Indiana State Board of Health has requested that the Indiana State Medical Association assist in its educational efforts, specifically in the following ways:

1. Joint teleconference through the IU network
2. Prepare and distribute a packet of AIDS information materials to (all or interested) ISMA members. ISBH will provide said materials
3. Identify ISMA members who will treat HTLV-III positive patients; Identify ISMA members who will treat AIDS patients (This information might be gleaned from a tear-out survey in ISMA REPORTS or INDIANA MEDICINE)

The above information would be available in a Resource Directory to be published by the Indiana State Board of Health in late 1986. ISBH has been awarded a grant for said directory.

4. Assist with distribution of directory, through county medical societies. Report availability of same in ISMA REPORTS and/or INDIANA MEDICINE
5. Woodrow Myers, M.D., Commissioner, Indiana State Board of Health, will write an updated article for INDIANA MEDICINE entitled "Current Knowledge on AIDS in Indiana"

Lawrence E. Allen, M.D., F.A.C.S. has been appointed to serve on the Indiana State Board of Health's AIDS Advisory Committee. This committee will attempt to identify a mechanism for legislation that will direct specific funding for AIDS as well as identify a means for approaching legislators on this issue. A further recommendation of the committee will involve total confidentiality. All AIDS patients' records MUST be totally confidential.

Ad Hoc Indigent Care Committee

Submitted by: Lawrence E. Allen, M.D., Chairman
Referred to: Reference Comm. 5

The Chairman met with Mr. Donald Blinzinger, Administrator, Indiana Department of Public Welfare, and Woodrow Myers, M.D., Commissioner, Indiana State Board of Health, to discuss health care for the indigent.

The 1986 Indiana General Assembly did give hospital care to the indigent.

As the reality of the 1987 session of the Indiana General Assembly will be an attempt to balance the budget, additional spending is unlikely. It is believed additional monies will not be available for indigent health care. It is unlikely that the legislation is going to request an increase on the alcohol or tobacco tax, or to ask for a premium (insurance) tax.

There is no way to expand the role of Medicaid without adding to the funding mechanism.

Three possible ways of changing attitudes regarding health insurance were identified as:

1. The small employer (employing 50-109 people) could be given a tax incentive for insuring his employees (or could be penalized for not insuring same)
2. Another group of medical needy is the individual who does not (financially cannot) insure himself adequately
3. Insurance coverage should continue for one year following employment (allowing coverage for lay-offs)

Pertinent questions regarding the medical needy (indigent):

1. How many people are medical needy?
2. Where are they located?
3. Who are they?
   a. the young
   b. the old
   c. families
4. How much are they costing us?

The critical stand for ISMA, the physician community, is to stay "plugged into" the issue of the medical underinsured. It is important to keep visible regarding this issue in the General Assembly, because it is the physician who will have to implement the program. Keeping the physician "plugged in" helps the Medicaid maintain diversity in its supporters and assists in keeping it all honest.

Woodrow Myers, M.D. is seeking an outside funding contract for appropriate funds for indigent care.

Lawrence E. Allen, M.D., F.A.C.S. has been appointed to the Governor's Subcommittee on Indigent Care. This is a subcommittee of the Steering Committee on Health Care for the Medical Underserved and is chaired by Mr. Ken Stella, Vice President, Indiana Hospital Association. Through this appointment, ISMA's further input into the planning is ensured.

Ad Hoc Committee on Geriatrics

Submitted by: B. L. Martz, M.D., Chairman
Referred to: Reference Comm. 5

The committee has stimulated the use of the TV series "Healthy, Happy and Wise" by various groups and agencies involved in programs for older Hoosiers. It is felt that greater promotion of these excellent video tapes is indicated. The issues which these programs address remain timely.

The committee, acting on behalf of the Association, has collaborated with the medical school and the Indiana Public Health Foundation in organizing and sponsoring a Geriatric Medicine symposium on October 2, 1986 in Indianapolis on Physical Activity, a Deterrent to Aging."

In view of the growth of the nursing home system and ever increasing need for greater physician participation in care in that setting, the committee felt it desirable to endorse the position paper developed by the American Geriatric Society.

1986 Physician Community Service Award

Robert W. Dettmer, M.D.
Fort Wayne

Dr. Robert W. Dettmer of Fort Wayne is the recipient of the 1986 Physician Community Service Award.

In the past year, in addition to his active practice in internal medicine and nephrology, Dr. Dettmer has undertaken almost single-handed leadership of two simultaneous campaigns to raise funds for the Three Rivers Neighborhood Health Service, Inc., a clinic that serves low-income residents of Fort Wayne-Allen County.

The clinic provides immunizations and health examinations for youngsters, and offers prenatal and family planning programs and a Medical Referral Service. In 1985 more than 500 women received prenatal care and there were more than 18,000 patient visits to the clinic.

Dr. Dettmer has devoted hundreds of volunteer hours on behalf of the clinic in an effort to establish a $1 million endowment to ensure future operating funds for clinic services, and a $1 million fund for renovation and relocation of the clinic to more spacious quarters in downtown Fort Wayne.

In May 1986, the Fort Wayne Medical Society (FWMS) presented Dr. Dettmer its first Humanitarian Service Award for his "perseverance, dedication and voluntary service."

Dr. Dettmer is a former FWMS president and recently completed a second term as chairman of the FWMS Board of Trustees. He was recently elected Board president of the Three Rivers Neighborhood Health Services. He is also a co-founder of a local chapter of the Christian Medical Society.

Dr. Dettmer and his wife Sue have four children, Kimberly, Shelley, Robert Jr., and Thomas.



Dr. Dettmer and his wife Sue.

Carrie Jackson
Television
(Single Story & Series)

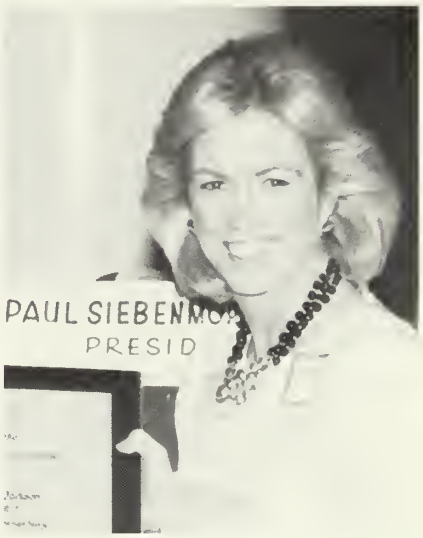
Carrie Jackson, Indianapolis, former news co-anchor at WTHR, won in the TV-Single Story category with her entry, "Cost of a Cure." The story concerned research into Duchenne's Muscular Dystrophy being conducted by Dr. Charles A. Bonsett, chief of neurology at Community Hospital, Indianapolis.

Ms. Jackson also won in the TV-Series category with her entry, "AIDS: Fact or Fiction?" The series aired in January 1986 and coincided with the State Board of Health's AIDS Awareness Week. The series was intended to dispel hysterical myths and educate the public about how one gets AIDS, who gets it, and how to avoid getting it.

Ms. Jackson, who previously won in the TV-Series category in 1984, is now director of the Bureau of Health Promotion for the Indiana State Board of Health.

Entries for the annual ISMA Journalism Awards competition must be submitted to ISMA headquarters through the county medical society.

Entries are judged (by the Commission on Public Relations) on the basis of health and medical accuracy, significance, quality, interest and impact on the general public.



Carrie Jackson



Jan Sherbin

Pat Cline
Print (Series)

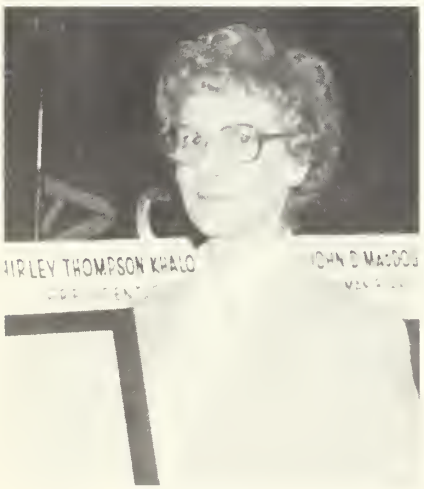
Pat Cline, civic affairs editor of the *Crawfordsville Journal Review*, won in the Print-Series category with her entry, "Impact of Medicare System Changes." The three-part series, which appeared in the *Journal Review* Feb. 20-22, 1986, reported on recent Medicare changes and what impact they will have on the cost and quality of health care.

Ms. Cline has received numerous media and service awards and belongs to several professional and civic organizations, including Sigma Delta Chi and the Women's Press Club of Indiana.

Jan Sherbin
Radio

Jan Sherbin, formerly news director of WAJI-FM, Fort Wayne, won in the Radio category with her entry, "Inside the Mind of a Drunk Driver." The 10-part series, which aired in August 1985, examined the problem of drunk driving and contained a candid interview with a former drunk driver who was responsible for two traffic deaths.

Ms. Sherbin, now manager of video and printed communications for Procter & Gamble, Cincinatti, has won reporting awards from the AP, UPI, the National and Indiana American Legion auxiliaries, and the American Chiropractic Assn.



Pat Cline



Sam Stall

Sam Stall
Print (Single Story)

Sam Stall, an Indianapolis journalist, won in the Print-Single Story category with his entry, "Change of Mind," published in *Indianapolis Monthly* magazine in November 1985. His article illustrated the effects of Alzheimer's disease on the sufferer, and family and friends of the sufferer.

Mr. Stall is a staff writer and special projects editor for *Indianapolis Monthly*. He is a graduate of Ball State University who won the 1986 Casper Community Service Award and several Indiana Collegiate Press Association awards.

Resolutions

RESOLUTION 86-1
Submission of Resolutions to the House of Delegates
Introduced by: Commission on Constitution and Bylaws
Referred to: Reference Committee 2
ACTION: ADOPTED AS AMENDED

Whereas, Section 3.020701 of the ISMA Bylaws is not clear as to who shall be entitled to submit resolutions to the House; and

Whereas, The Commission on Constitution and Bylaws believes it is appropriate that only members of the House of Delegates be entitled to submit resolutions; therefore be it

RESOLVED, That Section 3.020701 be modified as set forth below:

"3.020701 Resolutions and Proposals: Only members of the Indiana State Medical Association may sponsor resolutions to the House of Delegates. The House of Delegates shall approve all memorials and resolutions issued in the name of the Association before same shall become effective.

RESOLUTION 86-2
Formation of Physician and Family Support Group
Introduced by: Fort Wayne Medical Society Board of Trustees
Referred to: Reference Committee 5
ACTION: ADOPTED

Whereas, the psychological trauma a physician and his/her family experiences during a professional liability suit process is a matter of growing recognition and concern within the medical community; and

Whereas, physicians and their families react to the stress of litigation in a multiplicity of ways; and

Whereas, the emotion, feelings and fears elicited are commonly shared by physicians and their families as each in their own way works through the process; therefore be it

RESOLVED, That the Indiana State Medical Association provide the leadership and support to facilitate the formation of district and/or county Medical Society Physician-Family Support Groups, to provide assistance, emotional support, information and listening to physicians and their families going through a malpractice suit.

Fiscal Note: $500.00

RESOLUTION 86-3
Fifty Year Club
Introduced by: ISMA Editorial Board of INDIANA MEDICINE
Referred to: Reference Committee 2
ACTION: ADOPTED

Whereas, The ISMA Bylaws presently do not officially recognize the Fifty Year Club or provide appropriate instruction concerning the annual meeting of the "Club;" therefore be it

RESOLVED, That the ISMA Bylaws be amended to include a section recognizing the Fifty Year Club and provide appropriate instruction concerning the annual meeting of the "Club."

RESOLUTION 86-4
Bylaw Changes Relating to INDIANA MEDICINE
Introduced by: ISMA Editorial Board of INDIANA MEDICINE
Referred to: Reference Committee 2
ACTION: ADOPTED

Whereas, Publication in INDIANA MEDICINE of reports and documents relating to official acts of the ISMA has been governed, in the past, by partial instructions in the Bylaws together with various customs of unknown origin; and

Whereas, It has been the opinion of the Executive Committee that many of the matters contained in the Bylaws should be removed and included as Editorial Policy rather than as part of the Bylaws; therefore be it

RESOLVED, That the following sections of the ISMA Constitution and Bylaws be amended as follows:

3.021101 Reference Committees: Immediately after the organization of the House of Delegates at each Annual Convention, the Speaker shall announce the membership of the Reference Committees to serve during the convention for which they are appointed.

Appointments to these Reference Committees shall be made by the Speaker. The Chairman of each committee shall also be appointed by the Speaker. The Speaker shall also appoint such additional House committees as the House may approve. All committees hereunder shall serve only during the convention at which they are appointed. ~~Appointments shall be made in time to be published in INDIANA MEDICINE and the Handbook prior to such Annual Convention.~~

5.0606 County Visitation, Expenses and Reports: Each Trustee shall be organizer, peacemaker, and censor for the represented district. The Trustee shall visit the counties in the represented district at least once a year for the purpose of organizing component

societies where none exist; for inquiring into the condition of the profession, and for improving and increasing the zeal of the county societies and their members. The Trustee shall make an annual report of official work and of the condition of the profession of each county in the represented district. ~~the same to be published in the number of INDIANA MEDICINE which is issued immediately preceding the Annual Convention . . .~~

7.1008 The Commission on Convention Arrangements: The commission on Convention Arrangements, with the advice and assistance of the Executive Director, shall provide suitable accommodations for meetings of the Association, including the House of Delegates, Board, and of their respective committees, the scientific and technical exhibits, and in conjunction with the Executive Director, shall have general charge of all the arrangements. Its Chairman shall report an outline of the arrangements to the Executive Director of the Association for publication ~~in INDIANA MEDICINE and~~ in the official program, and shall make additional announcements during the session as occasion may require . . .

RESOLUTION 86-5
Purchase of IPRO Stock by ISMA
Introduced by: ISMA Board of Trustees
Referred to: Reference Committee 5
ACTION: NOT ADOPTED

Whereas, IPRO has converted to for-profit status; and

Whereas, ISMA may have the opportunity to purchase stock in IPRO and be in a position to elect members to the Board of Directors of the for-profit corporation; therefore be it

RESOLVED, That the Indiana State Medical Association House of Delegates determine whether or not ISMA should take advantage of any future offers from IPRO to purchase stock in the for-profit corporation.

ISMA Fiscal Note: $27,000 (Estimated expense for 225 shares @ $120 each)

RESOLUTION 86-6
Medical Legal Compact of Conduct of the Indiana State Bar Association and Indiana State Medical Association
Introduced by: ISMA Board of Trustees and ISMA Medico-Legal Committee
Referred to: Reference Committee 5
ACTION: ADOPTED

Whereas, The Indiana State Bar Association and the Indiana State Medical Association has been working for a number of years to arrive at a code of conduct that can be supported by both organizations; and

Whereas, the current draft of the compact has been reviewed and approved by the ISMA Medico-Legal Committee, the Executive Committee, and the Board of Trustees; therefore be it

RESOLVED, That the Indiana State Medical Association House of Delegates approve and adopt the "Medical Legal Compact of Conduct of the Indiana State Bar Association and Indiana State Medical Association."

(Note: The Compact appears verbatim on page 100 of this issue.)

RESOLUTION 86-7
Quality Medical Care
Introduced by: Delaware/Blackford County Medical Society
Referred to: Reference Committee 4
ACTION: ADOPTED AS AMENDED

Whereas, The physicians of Indiana realize that quality medical care for the patient is the most important service they offer; and

Whereas, The delivery of medical care is in the process of being changed drastically with the emphasis on cost containment rather than on quality medical care; therefore be it

RESOLVED, That physicians of Indiana will not comprise the quality of medical care because of financial incentives.

RESOLUTION 86-8
Military Physicians
Introduced by: Board of Trustees
Referred to: Reference Committee 2
ACTION: ADOPTED AS AMENDED

Whereas, Resolution 85-2 passed the 1985 House and was referred to the Board of Trustees with subsequent report to the 1986 House of Delegates; and

Whereas, the Board of Trustees referred Resolution 85-2 to the Commission on Constitution and Bylaws for suggestions as to verbiage; therefore be it

RESOLVED, That Section 1.01 be amended as follows:

"1.01 CATEGORIES: Categories of membership are: 1) Regular; 2) Dues Exempt; 3) Resident; 4) Medical Student; 5) Distinguished; 6) Honorary; 7) Military."

RESOLVED, That the following language be added to the Bylaws as Section 1.0107 as follows:

"1.0107 MILITARY: Any physician-member of the active duty military service stationed in Indiana (not to include physicians in the Reserve

on temporary active duty) shall be permitted to join a component medical society of ISMA and become a member of ISMA at reduced dues that shall be determined by the Board of Trustees."

RESOLUTION 86-9
Education of Physicians in Utilization and Quality Review Matters
Introduced by: S. Rahim Farid, M.D. and W. L. Strecker, M.D.
Referred to: Reference Committee 4
ACTION: ADOPTED AS AMENDED

Whereas, The importance of utilization review and quality assurance activities has never been greater than it is today. Required Medicare review activities, carried out by local doctors through contracts with peer review organizations, have made a tremendous impact on the practices of all primary care physicians. Private industry and third party payors have also responded, in significant numbers and with strong measures, to the pressures of increasing health care costs in economically-troubled times; and

Whereas, Today there is no question that cost containment and quality assurance is here to stay. The basic objective, a health care system that provides the best care possible at a cost that we as a nation can afford, is one that we can all support as physicians. It is time for us, as a profession, to recognize that the complexity of appropriate review services requires a complete knowledge of medicine, health care data, and practice patterns. Only physicians are fully licensed and qualified to recognize health care which fails to meet standards of acceptability; and

Whereas, Physicians who have not played an active role in the design and implementation of review activities are ill-prepared for the task of providing care in an environment that is controlled and regulated by peer review processes. The complexity and multiplicity of these processes, coupled with complex payment and coverage policies administered by countless self-insured corporations and third party payors, including the federal government, wreak havoc in the doctor's office and discourage participation in activities sponsored by those who may seem to be the perpetrators of the problems; and

Whereas, Only licensed physicians who maintain an active practice in cognitive or procedural medicine or osteopathy are qualified to evaluate or review practices of their peers; and

Whereas, There exists no organized educational programs in any level of medical school, residency program, or post graduate continuing medical education program; and

Whereas, Health care cost containment and quality assurance activities are accepted as measures which are essential to the practice of medicine and are, in fact, a part of the daily routine of the practice of medicine; therefore be it

RESOLVED, That the Indiana State Medical Association, through the state network of physicians who form the foundation of this great organization, facilitate the development of a model program to introduce the field of utilization review and quality assurance for use by medical schools and programs of continuing medical education; therefore be it further

RESOLVED, That ISMA seek to encourage participation in review processes in all medical schools; therefore be it further

RESOLVED, That ISMA submit this resolution to the American Medical Association for consideration and implementation.

Fiscal Note: Undetermined

RESOLUTION 86-10
Return Investigation of Medical Complaints to the Indiana Board of Medical Licensing
Introduced by: Arthur G. Blazey, M.D.
Referred to: Reference Committee 3
ACTION: NOT ADOPTED

Whereas, Lawyers have been the majority of members elected to State Assemblies and to the Congress of the United States of America for many years; and

Whereas, That majority has assisted in the passage of unconstitutional laws for the past half century that have gradually reduced the value of the 1933 dollar to less than a nickel for the current unbacked Federal Reserve script; and

Whereas, They have passed laws in the Indiana General Assembly, or through the Indiana Register, that places the investigation of complaints made to the Indiana Medical Licensing Board (MLB) in the hands of the Indiana Attorney General's Office; and

Whereas, The Indiana Bar Association through the Disciplinary Commission of the Indiana Supreme Court maintains absolute control over who they will punish and they will not punish that can be injurious to the public interest; therefore be it

RESOLVED, That the ISMA Commission on Legislation present the Indiana General Assembly with a bill to amend such portions of the Indiana Code that give the Attorney General the authority to investigate complaints made to the MLB, and return that authority to the MLB.

RESOLUTION 86-11
Multiple Defendant Litigation
Introduced by: John Beeler, M.D., Chairman, Medico-Legal Committee
Referred to: Reference Committee 3
ACTION: ADOPTED

Whereas, In many instances plaintiffs' attorneys file malpractice cases against multiple defendants, due at least in part to their failure to properly investigate the case and determine who the appropriate defendants should be; and

Whereas, The filing of multiple defendant litigation has caused needless waste of time and money by those physicians who should have not been included in the litigation in the first place; therefore be it

RESOLVED, That the Indiana State Medical Association investigate the frequency and severity of multiple defendant litigation and take appropriate steps to resolve the problem.

RESOLUTION 86-12
Mandated Quarterly District Meetings
Introduced by: Eighth District Medical Society
Referred to: Reference Committee 2
ACTION: NOT ADOPTED

Whereas, The County Medical Society Officers, Trustee and Alternate Trustee of the Eighth District Medical Society believe there is a need to meet more frequently than once a year to discuss issues and to plan the program for the annual meeting; and

Whereas, It is our opinion that quarterly meetings would generate better communication between the counties in the Indiana State Medical Association Districts and help bring issues, in the form of resolutions, to the ISMA House of Delegates; and

Whereas, Quarterly meetings would better prepare the Trustee(s) and Alternate Trustee(s) to represent the thinking of his/her constituents at the ISMA Board of Trustees meetings; therefore be it

RESOLVED, That this ISMA House of Delegates mandate quarterly meetings be held by the 13 Trustee Districts from this day forward.

RESOLUTION 86-13
ISMA Opposition to School-Based Health Clinics
Introduced by: Robert L. Rudesill, M.D.
Helen B. Barnes, M.D.
John E. Ramsey, M.D.
Referred to: Reference Committee 3
ACTION: ADOPTED SUBSTITUTE RESOLUTION AND REFERRED TO THE BOARD OF TRUSTEES FOR IMPLEMENTATION

RESOLVED, That the issue of school-based health clinics is a complex problem requiring further investigation with the concerns of parental rights, the potential of inferior health care, lack of continuity of care, optimal use of existing programs, and failure of in-school clinics to impact statistically on the problem of adolescent health.

RESOLUTION 86-14
Coalition for a Tobacco-Free Society
Introduced by: Commission on Public Relations
Referred to: Reference Committee 5
ACTION: ADOPTED

Whereas, The Indiana State Medical Association, by vote of its 1985 House of Delegates, determined to support the efforts of the American Medical Association to work for a tobacco-free society by the year 2000; and

Whereas, The Indiana State Medical Association has established a Coalition for a Tobacco-Free Society made up of interested health-related groups and individuals; and

Whereas, The purpose of the coalition will be to promote public awareness of the hazards of tobacco use through the media, school visits with third and fourth grade students, and legislative efforts; therefore be it

RESOLVED, That the Indiana State Medical Association support the activities of the Coalition for a Tobacco-Free Society.

RESOLUTION 86-15
Tobacco-Free Society
Introduced by: Commission on Public Relations
Referred to: Reference Committee 5
ACTION: ADOPTED

Whereas, The Indiana State Medical Association has established a Coalition for a Tobacco-Free Society to carry out the mandate of the 1985 House of Delegates; and

Whereas, Support for this effort is needed in all counties of the State of Indiana; therefore be it

RESOLVED, That component county medical societies be encouraged to form local chapters of the coalition and to establish local activities to promote a Tobacco-Free Society.

RESOLUTION 86-16
Procedures of Medical Licensing Board
Introduced by: Mark M. Bevers, M.D., Fourth District Trustee
Referred to: Reference Committee 3
ACTION: ADOPTED AS AMENDED

Whereas, The Indiana Medical Licensing Board (MLB) has the authority under Indiana Statute to summarily suspend a practitioner's license if the MLB finds that the practitioner represents a clear and immediate danger to the public health and safety; and

Whereas, There are no requirements that the Medical Licensing Board notify the practitioner prior to the release of this action by the Board; and

Whereas, Under current practice of the MLB, a physician's license may be summarily suspended and

the physician may first find out of the action through the news media rather than by a notification from the MLB directly; therefore be it

RESOLVED, That the ISMA Board of Trustees suggest to the Medical Licensing Board a formal protocol for notification to practitioners prior to the public release of action taken by the MLB including summary suspensions; and be it further

RESOLVED, That information regarding the functions of the Medical Licensing Board be transmitted to ISMA members through an appropriate vehicle.

RESOLUTION 86-17
Organ Transplant Task Force
Introduced by: Fort Wayne Medical Society
Referred to: Reference Committee 5
ACTION: ADOPTED AS AMENDED

Whereas, The City of Fort Wayne has been a leader in organ recovery for transplant usage in the State of Indiana; and

Whereas, The City of Fort Wayne has pioneered cardiac transplant in northeastern Indiana; and

Whereas, Cardiac transplants are best done near the home of the patient for optimal results; and

Whereas, The Governor's Task Force on Transplantation does not adequately represent all areas of Indiana; therefore be it

RESOLVED, That the Indiana State Medical Association resist any efforts to restrict organ transplantation to a central location; therefore be it further

RESOLVED, That the Indiana State Medical Association actively promote the representation of appropriate major metropolitan areas on the Governor's Task Force.

RESOLUTION 86-18
Mail Order Prescriptions
Introduced by: Fort Wayne Medical Society
Referred to: Reference Committee 3
ACTION: ADOPTED AS AMENDED

Whereas, Employee contracts frequently mandate mail order prescriptions and increasingly "require" a minimum of a ninety (90) day supply; and

Whereas, In the practice of medicine, a number of patients represent a potential risk of overdose and for many patients, controlled quantities, controlled refill numbers and refill intervals are essential; and

Whereas, The prescribing and dispensing of a 90-day supply of drugs such as Valium or Cortisone to some patients could be dangerous or fatal; and

Whereas, The unwarranted accumulation of medication may lead to illicit diversion and usage of drugs; and

Whereas, This "fixed quantity, mail order" policy economically discriminates against patients who must pay "out of their own pockets" when the strict prescribing criteria cannot be met; therefore be it

RESOLVED, That the Indiana State Medical Association meet with the Indiana State Pharmaceutical Association and jointly communicate our concerns regarding quality of care issues that relate to mail order prescriptions to industry, insurance carriers, and the appropriate regulatory bodies, and be it further

RESOLVED, That the Indiana AMA Delegation present this issue to the full AMA House of Delegates for consideration.

RESOLUTION 86-19
ISMA-HMSS Model Medical Staff Bylaws
Introduced by: Indiana State Medical Association Hospital Medical Staff Section
Referred to: Reference Committee 2
ACTION: ADOPTED AS AMENDED

Whereas, There is a statewide need for assistance in dealing with Hospital Medical Staff Bylaws; and

Whereas, The ISMA-HMSS has worked this past year to prepare a model Hospital Medical Staff Bylaw document; and

Whereas, The model document has been approved by the ISMA-HMSS and the ISMA Board of Trustees; therefore be it

RESOLVED, That this House of Delegates approve the "model" Hospital Medical Staff Bylaws as an official ISMA document to be available to hospital medical staffs and that the model bylaws be subject to annual review by the Hospital Medical Staff Section.

RESOLUTION 86-20
Indiana State Board of Health Radiologic Health Program
Introduced by: Indiana State Medical Association Hospital Medical Staff Section
Referred to: Reference Committee 3
ACTION: ADOPTED

Whereas, The Indiana State Board of Health Radiologic Health Program exists to protect the citizens of our state from needless radiation exposure; and

Whereas, Radon gas has been identified as a substantial newly recognized threat to some citizens of our state; and

Whereas, At least five nuclear power plants in Michigan and Illinois could in the event of a nuclear accident pose a significant risk to some citizens of our state; and

Whereas, Current Indiana law mandates a radiation machine operators certification program and a

radiation machine inspection program; therefore be it

RESOLVED, That the Indiana State Medical Association support improved staffing and funding of the Radiologic Health Division of the Indiana State Board of Health to provide technical assistance and monitoring of real and potential radiation threats throughout Indiana.

RESOLUTION 86-21
HMSS Vote in ISMA House of Delegates
Introduced by: Indiana State Medical Association Hospital Medical Staff Section
Referred to: Reference Committee 2
ACTION: NOT ADOPTED

Whereas, The Hospital Medical Staff Section of the Indiana State Medical Association is composed of one representative and one alternate representative appointed, or otherwise selected from the medical staff of each licensed hospital in Indiana; and

Whereas, The ISMA-HMSS constitutes true grass roots representation of hospital medical staffs to the ISMA; and

Whereas, The ISMA-HMSS assures the same vote for a small hospital as for a large hospital in a manner comparable to the unit vote allotted individual states by the composition of the United States Senate, irrespective of the population of the states represented; and

Whereas, Inasmuch as the ISMA in providing a voice for the physicians of Indiana, individually and collectively, should also provide a voice for the actively practicing physicians who constitute the medical staffs of Indiana hospitals; and

Whereas, The ISMA-HMSS is constituted in a manner totally different from all other sections of the ISMA in that it represents no single specialty interest, but the interests of all; and

Whereas, The nature of a democratic organization demands that it be given a vote in the democratic process; and

Whereas, The House of Delegates of the American Medical Association recognizing the aforementioned admits a delegate with full voting privileges from the AMA-HMSS to its chambers; therefore be it

RESOLVED, That the House of Delegates of the Indiana State Medical Association admit a delegate (and alternate) with full voting privileges from the ISMA-HMSS Section.

RESOLUTION 86-22
Prescription Abuse Data Synthesis (PADS) Program
Introduced by: Edward L. Langston, M.D.
Referred to: Reference Committee 3
ACTION: ADOPTED

Whereas, The AMA's House of Delegates has responded to the growing problem of the illegal diversion of prescription drugs through the creation of the Prescription Abuse Data Synthesis program; and

Whereas, Federal statistics have proven that the abuse of prescription drugs results in more injuries and deaths than all illegal drugs combined; and

Whereas, The AMA has made available to the state medical societies a comprehensive interprofessional program to study the prescription drug diversion problem and to improve the prescribing and dispensing practices of all health professionals; and

Whereas, Several states have implemented the PADS program whereby state and law enforcement officials and health professionals use existing information to target the sources of prescription drug diversion; therefore be it

RESOLVED, That the PADS program be implemented in Indiana and that the ISMA lend its full cooperation to this program's implementation; therefore be it further

RESOLVED, That the ISMA educate the physicians of this state on the various methods of illegal prescription drug diversion.

RESOLUTION 86-23
Pan American Games
Introduced by: Commission on Sports Medicine
Referred to: Reference Committee 4
ACTION: ADOPTED

Whereas, Indiana will be the host state (with Indianapolis and Michigan City as host cities) to the Tenth Pan American Games in August, 1987; and

Whereas, The Pan American Games are a major amateur athletic event, second in importance and prestige only to the Olympics; and

Whereas, Thirty-seven countries and approximately 5,000 athletes will compete in these Games; and

Whereas, 1987 has been designated the "Year of the Americas" with the highlight to be the Pan American Games in Indiana; and

Whereas, A safe, healthy environment is the goal of every sporting event in Indiana; and

Whereas, The budget to provide medical services, including doping control and gender verification, is severely limited; therefore be it

RESOLVED, That the Indiana State Medical Association is committed to assist the local organizing committees in their efforts to provide quality medical services to the athletes, support personnel, volunteers, and spectators of these Games; therefore be it further

RESOLVED, That ISMA will encourage its members to volunteer their services wherever possible in support of the Games without consideration for financial gain and with the best of ethical standards; therefore be it further

RESOLVED, That ISMA wishes to foster better understanding and communication between the Pan American countries and their medical communities and will, therefore, seek assistance from the Medical Licensing Board, Physicians Insurance Company of Indiana, and other appropriate agencies to aid our foreign physician counterparts who will visit Indiana in support of their respective teams.

RESOLUTION 86-24
Use of Protective Headgear During Equestrian Activities
Introduced by: Commission on Sports Medicine
Referred to: Reference Committee 3
ACTION: ADOPTED AS AMENDED

Whereas, Horseback riding accidents are one of the leading causes of accidents from recreational activities; and

Whereas, These accidents are a serious cause of head injuries with resultant death or permanent residual effects; therefore be it

RESOLVED, That the Indiana State Medical Association encourage educational programs to be given to parents, riding instructors, show organizers, and managers outlining the risks of horseback riding and methods to minimize them; therefore be it further

RESOLVED, That the Indiana State Medical Association recommend that a satisfactory protective headgear, which can pass standards for retention, penetration, absorption and distribution of shock be selected for each type of riding activity and worn when riding or preparing to ride; therefore be it further

RESOLVED, That the Indiana State Medical Association recommend that riding schools, horse shows, rodeos, and other equestrian events be urged to require that protective headgear be worn during the activities and that this issue be presented by the Indiana AMA Delegation to the full AMA House of Delegates.

RESOLUTION 86-25
Constitution and Bylaws Changes
Introduced by: Fountain-Warren County Medical Society
Referred to: Reference Committee 2
ACTION: FIRST RESOLVE ADOPTED; SECOND RESOLVE NOT ADOPTED

Therefore be it

RESOLVED, That effective in 1988 the Commission on Constitution and Bylaws remove the bylaw language which permits the President of ISMA to introduce resolutions to the House during the annual President's address; therefore be it further

RESOLVED, That the Commission on Constitution and Bylaws remove the bylaw language which prevents a major officeholder from holding more than one major office.

RESOLUTION 86-26
Passage of Tobacco-Free Society Legislation
Introduced by: Commission on Legislation
Referred to: Reference Committee 5
ACTION: ADOPTED AS AMENDED

Whereas, The ISMA's House of Delegates in 1985 adopted a resolution to move Indiana towards a Tobacco-Free Society by 2000; and

Whereas, The incidence of tobacco use especially smokeless tobacco by Indiana's youth has risen significantly; and

Whereas, The use of tobacco and the effects of secondhand smoke clearly are public policy matters; and

Whereas, Indiana's lawmakers should be asked by the ISMA to consider placing into Indiana law measures that are designed to help to reduce the incidence of tobacco use; therefore be it

RESOLVED, That the ISMA exert legislative effort to secure statutory enactment of proposals designed to:

1. Raise the minimum age in Indiana for purchase of tobacco from the present age of 16 to age 21;
2. Restrict smoking in any buildings owned or leased by any governmental unit;
3. Restrict smoking in any health facility licensed in Indiana; and
4. Prohibit the distribution of tobacco products free of charge on public streets or sidewalks, in public buildings, or in any public facility.

RESOLUTION 86-27
Anabolic Steroids
Introduced by: Commission on Sports Medicine
Referred to: Reference Committee 4
ACTION: ADOPTED

Whereas, There is controversial evidence of the benefits of anabolic steroids; and

Whereas, There are ever present potential dangers involved in the usage of anabolic steroids; and

Whereas, Certain governing bodies in athletics have rules against the use of such drugs; therefore be it

RESOLVED, That the Indiana State Medical Association completely and officially oppose the use of anabolic steroids as a method of enhancing athletic performance at all levels in sports.

RESOLUTION 86-28
Medicare Treatment of First-Year Physicians During the Fee Freeze
Introduced by: Thomas A. Barley, M.D.
Referred to: Reference Committee 3
ACTION: SUBSTITUTE RESOLUTION ADOPTED

RESOLVED, That the ISMA protest the specific discrimination towards physicians, entering practice since 1984, by being placed in the 50th percentile of prevailing rates at the initiation of their practice for up to 15 months and thus creating a hardship for their patients. Further, that ISMA be directed to inform the Health Care Financing Administration, and Otis R. Bowen, M.D., Secretary of Health and Human Services, as well as the Indiana Congressional and Senate Delegation of this unfair action by HCFA.

RESOLUTION 86-29
Communications Between Constituent Societies
Introduced by: Lake County Medical Society
Referred to: Reference Committee 5
ACTION: NOT ADOPTED

Whereas, Communications now and in the future are of key importance in medical practice and in medical societies; and

Whereas, The benefit to the citizens of the State of Indiana for a high level of technical communications would greatly assist medical practice; and

Whereas, Such communications between state and constituent counties and among constituent societies would be of immeasurable benefit; therefore be it

RESOLVED, That ISMA allocate from its public relations budget an amount to assist all constituent societies to purchase computer equipment necessary to allow a system of inter-communications; therefore be it further

RESOLVED, That all such equipment be compatable such that inter-communications can occur; therefore be it further

RESOLVED, That assistance be provided only on a participating basis to assure a constituent society commitment.

FISCAL NOTE: One time cost—$7,000
Annual maintenance—$1,000
ISMA FISCAL NOTE: $64,000 ($4,000 per installation for 16 counties)
$ 4,800 ($300 per installation a year for maintenance)

RESOLUTION 86-30
Prohibit Liability Suits Against Physicians Treating Medicaid Patients
Introduced by: Lake County Medical Society
Referred to: Reference Committee 3
ACTION: NOT ADOPTED

Whereas, Liability for physicians can occur in any area of practice; and

Whereas, Physicians contribute time and effort to caring for patients on Medicaid, HCI, and hospital emergency room care for indigents; and

Whereas, Much of this care is rendered at no charge or substantially reduced charge or by payment from publicly funded programs; and

Whereas, Costs of overhead, including liability insurance, cannot be fairly recovered under such low payment programs; and

Whereas, It is in the public interest to encourage physician participation in indigent care programs; therefore be it

RESOLVED, That ISMA support legislation to prohibit liability suits (or to provide primary coverage out of the Patient's Compensation Fund) for any physician rendering care to a patient covered by Medicaid, HCI, or township trustee, in a hospital emergency room, or in any setting in which it is determined (in advance) that care is to be provided for no charge to the patient.

RESOLUTION 86-31
Public Notice of Medical Liability Insurance Rate Changes
Introduced by: Lake County Medical Society
Referred to: Reference Committee 3
ACTION: ADOPTED AS AMENDED

Whereas, Liability insurance rates in Indiana are subject to change simply upon notice by insurance company to Insurance Commissioner; and

Whereas, Changes are not subject to fair public notice through the *Indiana Register* or comparable publication; and

Whereas, Rates can be increased or can discriminate among areas without opportunity for fair notice and full public comment by those affected; and

Whereas, Public comments should be encouraged to assure fair treatment of all concerned; therefore be it

RESOLVED, That ISMA support state legislation requiring public notice of medical liability insurance rate changes through the means of the *Indiana Register* and that such notice allow for public comment on changes prior to effectiveness of changes.

RESOLUTION 86-32
Uniform Rates for Liability Insurance
Introduced by: Lake County Medical Society
Referred to: Reference Committee 4
ACTION: ADOPTED AS AMENDED

Whereas, Recent acts by the Indiana Insurance Commissioner have allowed different premium rates

for medical specialties among geographic areas of Indiana; and

Whereas, Such differential in rates has not before been recognized in Indiana, which has always been a uniform rate state for purposes of medical liability rates; and

Whereas, Different rates are based on perceived actuarial characteristics of an area; and

Whereas, Characteristics are based upon levels, nature, and amounts awarded in law suits, both settled and pending; and

Whereas, Lawsuits are based upon state law and not local law; and

Whereas, Such lawsuits and underlying statutes are statewide in effect and can only be resolved on a statewide basis; and

Whereas, Discriminatory rates impose an unfair burden upon a part of the state by requiring higher rates and a disproportionately higher premium surcharge; therefore be it

RESOLVED, That the Indiana State Medical Association should continue its efforts to ensure that the Insurance Commissioner does not allow arbitrary or capricious changes in malpractice premium rates.

RESOLUTION 86-33
Funding to Constituent Societies for Statewide Programs

Introduced by:	Lake County Medical Society
Referred to:	Reference Committee 4
ACTION:	NOT ADOPTED

Whereas, Statewide programs are intended to benefit all ISMA members; and

Whereas, Such programs should be coordinated throughout the state; and

Whereas, Such coordination can best be accomplished when integrated into constituent society efforts; and

Whereas, Constituent societies are often best suited to provide the local or regional activities of a statewide coordinated plan; and

Whereas, It is in the best interest of the state to coordinate its efforts through those constituents able to assist and thereby to restrain costs, enhance efficiency, and have access to greater personal resources than could otherwise be attained; therefore be it

RESOLVED, That ISMA make available to such constituent societies as are able and willing, for purposes of carrying on the local or regional aspects of statewide programs, an amount allocated from the ISMA amounts budgets for such statewide programs; therefore be it further

RESOLVED, That amounts be allocated on a *per capita* basis for each ISMA member located in such locality or region; therefore be it further

RESOLVED, That allocated amounts be used exclusively for such purpose.

FISCAL NOTE: Undetermined

RESOLUTION 86-34
Dues for Constituent Societies

Introduced by:	Lake County Medical Society
Referred to:	Reference Committee 4
ACTION:	NOT ADOPTED

Whereas, ISMA bills dues for many constituent members; and

Whereas, Dues collected by ISMA for such societies is available to ISMA for its use until paid back to constituent; and

Whereas, Dues may collect interest for the period of time from collection until payment; and

Whereas, Such interest is on dues belonging to constituent; and

Whereas, Such interest likewise belongs to the constituent; therefore be it

RESOLVED, That ISMA forward on a monthly basis all interest earned on dues of constituent societies held by ISMA.

RESOLUTION 86-35
Guidelines for Second Medical Opinions

Introduced by:	Lake County Medical Society
Referred to:	Reference Committee 4
ACTION:	ADOPTED AS AMENDED

Whereas, Second medical opinions are required under many health insurance policies; and

Whereas, Method and procedures of such agencies vary between programs; and

Whereas, The medical benefit of a second opinion, if any, depends upon the procedure used to render medical opinion; and

Whereas, Guidelines would assure a common point of reference in second medical opinions; therefore be it

RESOLVED, That the Subcommission on Insurance of ISMA consider uniform guidelines for second surgical opinions in conjunction with similar efforts by the AMA; therefore be it further

RESOLVED, That such guidelines as adopted by the Board be distributed to all health insurers in Indiana, to the Indiana Insurance Commissioner, to all publicly financed health programs in Indiana, and to all ISMA members.

RESOLUTION 86-36
"Lay Midwives"

Introduced by:	LaGrange County Medical Society
Referred to:	Reference Committee 3
ACTION:	SUBSTITUTE RESOLUTION ADOPTED

RESOLVED, That ISMA recommends enforcement of existing laws that prohibit midwifery by unlicensed individuals.

RESOLUTION 86-37
Purchase of IPRO Stock
Introduced by: Vigo County Medical Society
Referred to: Reference Committee 5
ACTION: NOT ADOPTED

Whereas, Indiana Peer Review Organization, Inc. (IPRO) was formed in 1984 as a not-for-profit corporation by the cooperative effort of Indiana State Medical Association (ISMA), Indiana Foundation for Medical Care (IFMC), Indiana Medical Review Organization (IMRO) and Indiana Association of Osteopathic Physicians and Surgeons (IAOPS) to perform medical review for Medicare patients in the State of Indiana within the guidelines of federal law and regulations; and

Whereas, The organizations that established IPRO retain no formal means of control over IPRO nor have they received any reports, either financial or otherwise, from IPRO in the past; and

Whereas, It is believed by those involved in IPRO that the two physician-sponsored peer review organizations providing services in the State of Indiana prior to the PRO legislation (IFMC and IMRO) as well as all physicians in the State of Indiana, through their statewide organizations, should direct and control IPRO; and

Whereas, An attempt has been made to provide for such direction and control by changing IPRO to a for-profit corporation, with each of the forming organizations holding an appropriate share of the equity, and with each organization appointing members to the Board of Directors of IPRO in accordance with its share of equity; and

Whereas, any dividends issued by IPRO would be paid to organizations holding equity positions in accordance with the percentage of shares that they hold in IPRO; and

Whereas, The Board of Directors of IPRO will readily entertain an offer from ISMA to purchase stock in the corporation; therefore be it

RESOLVED, That the House of Delegates of ISMA instruct the Board of Trustees of ISMA to purchase up to 30% of the shares of the IPRO stock, and to exercise its share of the control over IPRO by appointing Directors that will be directly responsible to ISMA.

FISCAL NOTE: $20,000
ISMA FISCAL NOTE: $27,000 (Estimated expense for 225 shares @ $120 each)

RESOLUTION 86-38
$1.00 Increase in ISMA Dues to Assist the ISMA Auxiliary
Introduced by: Paul Siebenmorgen, M.D., President, ISMA
Referred to: Reference Committee 5
ACTION: NOT ADOPTED

Whereas, ISMA has consistently supported the efforts of the ISMA Auxiliary by allocating $1.00 of the ISMA dues to the Auxiliary; and

Whereas, It has come to the attention of ISMA that the Auxiliary is in need of additional financial support in order to finance its goals and objectives; therefore be it

RESOLVED, That ISMA dues be increased by $1.00 and allocated to the ISMA Auxiliary.

RESOLUTION 86-39
Immunizations
Introduced by: Edward L. Langston, M.D.
Referred to: Reference Committee 4
ACTION: ADOPTED AS AMENDED

Whereas, Immunizations have proven their worth when measured by medical economic benefit criteria; and

Whereas, The price of immunizations, i.e., flu vaccine, MMR, DPT, and oral polio (but not limited to these alone) has escalated rapidly to the private practicing physicians in this nation; and

Whereas, The increased cost for administration of the immunizations as measured by employee cost, medical malpractice coverage cost, and immunization cost has caused great strain on the distribution of the immunizations throughout the American society; and

Whereas, The immunization of our population has for the most part been borne by private practitioners in the past, but this may be changing in the future because of administrative cost; and

Whereas, Governmental units are able to purchase immunizations at a greatly discounted price compared to the private practitioner; therefore be it

RESOLVED, That the Indiana State Medical Association petition that private practicing physicians pay the same price for immunizations as governmental units and clinics; therefore be it further

RESOLVED, That the ISMA carry forth this resolution through all appropriate avenues and channels.

RESOLUTION 86-40
Sodium Contents of "Fast Foods"
Introduced by: Third District Medical Society
Referred to: Reference Committee 5
ACTION: SUBSTITUTE RESOLUTION ADOPTED

RESOLVED, That the ISMA encourage Indiana fast food restaurants to:

1. Reduce the amount of sodium and saturated fat in their food items;
2. Provide nutritional information about their food items to customers upon request; and
3. Offer similar low fat alternatives to the high sodium and saturated fat food items.

RESOLUTION 86-41
Ancillary Membership for Out-of-State Physicians

Introduced by:	Resident Medical Society
Referred to:	Reference Committee 2
ACTION:	NOT ADOPTED

Whereas, Physicians, residents, and medical students with interests in Indiana medicine, despite temporary or permanent residence out of the state, are ineligible for ISMA membership under the present membership categories; and

Whereas, Provision for an ancillary membership category would encourage these interests to the benefit of our state organization and to organized medicine as a whole; and

Whereas, Such interested physicians, residents, and medical students would be expected to bear the costs of mailing membership correspondence and ISMA publications to out-of-state locations through membership dues; therefore be it

RESOLVED, That ISMA establish an ancillary membership category collectively for out-of-state physicians, residents, and medical students.

RESOLUTION 86-42
Joint Membership for Dual Physician Families

Introduced by:	Resident Medical Society
Referred to:	Reference Committee 5
ACTION:	NOT ADOPTED

Whereas, Many ISMA members are married to physicians who are likewise ISMA members; and

Whereas, Several ISMA mailings, such as newsletters, solicitations, and INDIANA MEDICINE are redundant for some such members; and

Whereas, Such ISMA members might not desire such duplicate mailings; therefore be it

RESOLVED, That this ISMA House of Delegates call for an optional reduction in membership dues equal to the cost, or a fraction thereof, of such duplicate mailings for dual member families; therefore be it further

RESOLVED, That ISMA delete the names of members desiring this option from said mailing lists.

RESOLUTION 86-43
District Meetings Held at Annual Convention

Introduced by:	Mark Bevers, M.D., Fourth District Trustee
Referred to:	Reference Committee 2
ACTION:	NOT ADOPTED

Whereas, The ISMA's Annual Meeting is held in order to afford the members an opportunity to discuss important issues and matters of business to the ISMA as a whole; and

Whereas, The district societies comprise an integral component of the ISMA and serve as a conduit of information from the county societies to the ISMA; and

Whereas, The attendance at the annual district meetings would be increased if the meetings were held in conjunction with the ISMA's annual meeting; therefore be it

RESOLVED, That the district societies of the ISMA hold their annual meetings during the ISMA's annual meeting where the district meetings would be held as caucuses of the annual meeting and the district officers would be elected at the annual district meeting of the ISMA; therefore be it further

RESOLVED, That the district societies determine whether or not they want to hold their district meeting at the ISMA's annual meeting.

RESOLUTION 86-44
Regarding Resolution 85-8, "ISMA Membership Suspension as a Result of Medical Licensing Board Suspension"

Introduced by:	Board of Trustees
Referred to:	Reference Committee 2
ACTION:	REFERRED BACK TO THE BOARD FOR CLARIFICATION

Whereas, The 1985 House of Delegates *did not pass Resolution 85-8* but did refer it to the Board of Trustees for consideration by the Commission on Constitution and Bylaws; and

Whereas, The 1985 Reference Committee recommended that ISMA establish a "*restricted membership*" category for those members whose licenses have been *suspended*, with no change in termination of membership for those physicians whose licenses have been *revoked*; and

Whereas, It is the position of the Board of Trustees that the Reference Committee recommendations should be followed; therefore be it

RESOLVED, That Section 1.0303 of the Indiana State Medical Association Bylaws be amended by adding Subsection 1.030301 (underlined) as follows:

1.0303 Suspension or Revocation of License: No person whose license to practice medicine has been suspended or revoked

or who is under sentence of suspension or expulsion from a component society, or whose name has been dropped from its roll of members, shall be entitled to any of the rights or benefits of this Association or of a component county society, nor shall said person be permitted to take part in any of their proceedings until the license and/or county membership has been restored. This shall not apply to physicians who have surrendered their license because of retirement under the provisions of the Medical Practice Law.

1.030301 Restricted Membership: A member of the Indiana State Medical Association who has submitted himself to the ISMA Commission on Physician Impairment or a comparable county or hospital impaired physician committee, may continue as a restricted member of ISMA with full membership privileges, even after suspension of his license by the Medical Licensing Board so long as he is actively cooperating with all treatment prescribed by the appropriate impaired physician committee, and is making satisfactory progress in his rehabilitation. This section does not apply to a physician who has had his license "revoked" by the Medical Licensing Board.

RESOLUTION 86-45
Support and Promotion of Private Practice
Introduced by: Miami County Medical Society
Referred to: Reference Committee 6
ACTION: ADOPTED AS AMENDED

Whereas, The private practice of medicine on a fee-for-service basis is coming under ever increasing pressure from "alternative" methods of health delivery and reimbursement; and

Whereas, Such "alternative" methods are capable of generating difficult and troubling conflicts of interest for physicians; and

Whereas, Such conflicts of interest are likely to become more powerful with the ever increasing competition for patients; therefore be it

RESOLVED, That ISMA constantly support and promote the concept of the private practice of medicine on a fee-for-service basis regardless of any other methodology embraced by members of the organizations; therefore be it further

RESOLVED, That recognizing organized medicine should and does support a pluralistic system of health care delivery; nevertheless ISMA should stand ever ready to vigorously defend the traditional private practice, fee-for-service method or any other legitimate system when such is attacked from within or without organized medicine.

RESOLUTION 86-46
Activities of IMRO/IPRO
Introduced by: Vanderburgh County Medical Society
Referred to: Reference Committee 5
ACTION: ADOPTED

Whereas, The reviewing activities of IMRO/IPRO have resulted in DRG codes being changed after a physician has, by his signature, indicated that the DRG code originally assigned was, to the best of his knowledge, the correct DRG code; and

Whereas, Letters are being sent by IMRO directly to the patient advising the patient that unnecessary care or procedures were applied and that both the hospital and the physician knew that this care and/or procedure was unnecessary and would not be covered by Medicare; and

Whereas, The names of "offending" physicians are being recorded by IMRO; and

Whereas, Sanctions such as fines and/or Medicare denials would be reported to the Medical Licensing Board and then publicly announced; therefore be it

RESOLVED, That the ISMA assign to the appropriate commission charged with action, the task of identifying the actual legal authority, implications and consequences of the IMRO/IPRO activities and report to the Board of Trustees for action on a timely basis and that the Board of Trustees report to the membership on a regular basis.

RESOLUTION 86-47
Postoperative Care of Surgical Patients
Introduced by: Paul Honan, M.D.
Referred to: Reference Committee 4
ACTION: ADOPTED AS AMENDED

Whereas, The Indiana State Medical Association believes that the postoperative care of surgical patients constitutes the practice of medicine; therefore be it

RESOLVED, That the Indiana State Medical Association seek confirmation through appropriate agencies as to whether permitting persons who are not licensed to practice medicine in the State of Indiana to provide such care is a violation of the Medical Practice Act; therefore be it further

RESOLVED, That the Indiana State Medical Association encourage its membership to provide postoperative care in accordance with the ethics of the medical profession; therefore be it further

RESOLVED, That the Indiana State Medical Association encourage its membership to report to the Medical Licensing Board any violations of the standards of the practice of medicine.

RESOLUTION 86-48
Physician Health Officers
Introduced by: Everett Bickers, M.D., Indiana Public Health Physicians Asssociation
Referred to: Reference Committee 3
ACTION: ADOPTED

Whereas, Indiana law currently provides that a local health officer be a licensed physician; and

Whereas, There are sufficient licensed physicians available in Indiana to serve as local health officers; and

Whereas, The responsibilities and duties of the local health officer require that the local health officer have medical training; therefore be it

RESOLVED, That the ISMA continue to support statutory provisions that require that the local health officer be a physician with an unlimited license to practice medicine in Indiana.

Resolution of Commendation for Gilbert M. Wilhelmus, M.D.
ACTION: ADOPTED BY ACCLAMATION

Whereas, Gilbert M. Wilhelmus, M.D., was the President of ISMA during the passage of the historic Tort Reform of 1975 which created the Patient's Compensation Fund, limited health care providers' total liability to $500,000.00, created medical review panels to review claims of negligence and reduce the statute of limitation for tort claims to two years from the date of occurrence; and

Whereas, Dr. Wilhelmus then was appointed chairman, by Governor Otis R. Bowen, of the statutory medical malpractice study committee from 1975-1980; and

Whereas, Dr. Wilhelmus will continue to serve organized medicine as a member of the Medical Licensing Board of Indiana; and

Whereas, Gilbert M. Wilhelmus, M.D., has been an honorable, knowledgeable and dedicated leader of organized medicine at all levels, many times at great sacrifice; therefore be it

RESOLVED, That this 1986 House of Delegates extend its deepest appreciation to Doctor Gilbert M. Wilhelmus for his years of dedicated service to organized medicine at all levels; and therefore be it further

RESOLVED, That this resolution be forwarded to the American Medical Association House of Delegates for its recognition of Doctor Wilhelmus' years of conscientious and effective leadership at the AMA level.

Resolution of Commendation for Malcolm O. Scamahorn, M.D.
ACTION: ADOPTED BY ACCLAMATION

Whereas, Malcolm O. Scamahorn, M.D. has been a tireless, dedicated, and knowledgeable leader of organized medicine at all levels, many times at great sacrifice to self and family; and

Whereas, Doctor Scamahorn, after serving as an Indiana Delegate to the American Medical Association since 1969 has decided not to seek reelection; and

Whereas, As a Delegate he has distinguished the Indiana State Medical Association members and himself by serving as its Floor Leader, Vice Chairman AMA Council on Medical Service, Chairman AMA Reference Committee F 1975-76, Chairman AMA Reference Committee B 1982, member AMA Medical Liability Direct and Indirect Cost Committee, Member AMA Work Group on Health Resources, Health Policy Agenda for the American People; and

Whereas, Doctor Scamahorn will continue to serve organized medicine as a member of the Task Force on Long-Term Health Care Policies of Health Care Financing Administration; therefore be it

RESOLVED, That this 1986 House of Delegates extend its deepest appreciation to Doctor Malcolm O. Scamahorn, and his family, for his long years of dedicated service to organized medicine at all levels; therefore be it further

RESOLVED, That this resolution be forwarded to the American Medical Association House of Delegates for its recognition of Doctor Scamahorn's years of conscientious and effective leadership at the AMA level.

Medical Legal Compact of Conduct as Approved by the House

The ISMA House of Delegates adopted Resolution 86-6, "Medical Legal Compact of Conduct of Indiana State Bar Association and Indiana State Medical Association," during its final session Nov. 2.

The resolution (see page 88) was introduced by the ISMA Board of Trustees and the ISMA Medico-Legal Committee, chaired by Dr. John W. Beeler of Indianapolis.

The ISBA and ISMA had been working for several years on a code of conduct that could be supported by both organizations. That code, which follows, represents the culmination of those efforts.

MEDICAL LEGAL COMPACT OF CONDUCT OF THE INDIANA STATE BAR ASSOCIATION AND INDIANA STATE MEDICAL ASSOCIATION

I. PREAMBLE

The provisions of this Compact have been prepared and are intended as guides to assist members of the medical and legal profession in their increasing mutual professional association. As the knowledge and services of both professions are required so that the rights of individuals may be appropriately determined before various tribunals, it is advantageous to have a voluntary Compact of Conduct between physicians and attorneys. A Compact of Conduct can clarify and delineate uncommon language and common problems, and communicate to both the medical and legal professions the manner in which each can best serve the public and secure to its citizens the best medical and legal services obtainable.

The provisions of the Compact are not laws, but reasoned rules of conduct for members of the two professions, subject to the principles of medical and legal ethics and rules of law prescribed for their individual conduct. However, the Compact will serve its purpose if it promotes the public welfare, improves the practical working relationships of the two professions, and facilitates the administration of justice.

II. PHYSICIAN-PATIENT PRIVILEGE

A. The physician-patient privilege did not exist at common law. It was created by statute to encourage a patient to freely communicate with the physician. The privilege belongs to the patient. Unless the patient waives the privilege or consents to the physician's disclosure of information, the physician is prohibited from disclosing to others information obtained as a result of a physician-patient relationship. The privilege does not prohibit a physician from making reasonable, professional disclosures, i.e., when staffing the patient or consulting with others on care.

B. When a patient commences a law suit wherein the patient's medical condition becomes an issue (injuries arising from malpractice, auto collision, slip and fall), the patient is legally deemed to have waived any privilege regarding communications or records concerning the medical condition at issue. Although the patient has waived the privilege, a physician should require the patient's consent to records or information disclosure, unless ordered to make disclosure by Court order or other legal document.

III. MEDICAL EXAMINATIONS (Requested by Attorneys or Ordered by the Court)

A. General

1. The law provides that a party to a law suit may be required to undergo a medical examination by agreement of the opposing attorneys or under a court order. (Trial Rule 35)

2. When an appointment is made for the medical examination of a person, the physician sets aside a part of his day for that purpose. It is, therefore, important that attorneys exert their best efforts to insure that such appointments are kept. The attorney for the party to be examined should give explicit instructions to such party that the physician must be notified in ample time should it become impossible for the party to keep the appointment. The attorney should know and agree upon the fee arrangement of the physician in advance of the appointment. A physician may charge for a cancelled or missed appointment when the physician is unable to reschedule another patient for the cancelled or missed appointment time.

B. Scope of Examination

1. The scope of an examination may be limited by the agreement of the attorneys or the court order. The attorney requesting the examination has the obligation of notifying the doctor of any such restriction.

2. Subject to the above limitation, the physician may take a history and perform such examinations as may be advisable in his judgment to formulate an informed opinion regarding the nature and extent of the party's medical condition.

3. Inquiries by attorneys should not be made into matters not reasonably related to the legitimate scope of the medical examination and the physician who is so requested should decline to do so.

IV. WRITTEN MEDICAL INFORMATION (Prepared for Courts or Attorneys)

A. The Attorney

1. Requests for medical records or medical reports from a physician should be tendered within a reasonable time in advance of the need for the information.

2. Except as provided in paragraph IV(A)(3), the physician shall release medical records and/or a medical report if requested only to attorneys who are authorized to receive same by a signed patient authorization complying with the requirements of IC §16-4-8-1 *et seq.* It shall be presumed that a patient authorization presented by an attorney representing a party adverse to the patient was obtained with the knowledge of the patient's attorney.

3. The foregoing subsection notwithstanding, an attorney may, after suit is filed, and pursuant to Trial Rule 34 of the *Indiana Rules of Trial Procedure*, subpoena medical records from the physician.

4. The attorney requesting medical information should state the purpose for the information, the specific information needed (see IV(B)(4)), and identify particular matters which the physician should know or address. For example, the Social Security Administration has precise medical guidelines and values which establish disability and Workmen's Compensation matters require the expression of a permanent impairment rating.

B. The Physician

1. Medical Records. The physician should keep adequate records of pertinent information regarding the patient's medical history, diagnosis, prognosis and treatment.

2. A physician may not withhold medical information because a patient's balance on account remains unpaid. A physician can request that the actual total cost of medical records duplication or the fee for medical report preparation be paid at the time records or reports are delivered (See IC §16-4-8-3).

3. If a physician is retained by an attorney to conduct a complete medical examination and is unable to make a complete medical evaluation within the time required, he should notify the attorney. In this event, a preliminary report clearly designated as such may serve the attorney's needs until a complete evaluation can be rendered.

4. Content of Reports. The physician should prepare a medical report to comply with the attorney's request. A request should specify the information needed. The medical report may include:

(a) History. State the history obtained, from whom, and when if obtained during several consultations. State what the patient did or said as well as what the patient did not do or report.

(b) Physical. Report the findings and observations of the physical exam. Include lab results and X-ray interpretations as relevant. Again, negative findings or observations may be relevant.
(c) Medication. Past, present and future, as relevant.
(d) Treatment rendered.
(e) Diagnosis, Findings or Impressions. In addition to stating a diagnosis, finding or impression, the physician may want to note any unusual or unexpected findings with reference to a medical test, observation or experience. If follow-up care or treatment is recommended, include service to be performed, whether elective or otherwise, and reasonable cost.
(f) Consider attaching copies of relevant portions of the medical record to support the report.

V. **DEPOSITION** (Testimony Under Oath Outside of Court)

A. Deposition Defined

A deposition is the interrogation of a witness before a court reporter who is authorized to record the proceedings, by electronic or mechanical means, for later transcription and use. Attorneys and parties in the law suit as well as their consultants may be present. The witness may have counsel present. Since there is no judge present to arbitrate disputes, objections or other proceedings are orally stated for the record of later consideration. If requested to bring documents to the deposition, the witness may be interrogated regarding the documents and the documents may be introduced as a part of the deposition record. Arrangements can be made to attach copies of documents to the deposition so that the witness can retain the originals.

B. Time and Place

The time and place of a deposition is set by agreement among the attorneys and the witness. Effort is made to accommodate a physician's full office and hospital schedule. On occasion, late evening or weekend appointments are necessary to accomplish a deposition.

VI. SUBPOENAS

A. Subpoena

A subpoena issues from the clerk of the court in the county where a law suit is pending. The subpoena issues at the request of an attorney, who specifies time, date and place where the physician subpoenaed must be. The attorney should not subpoena a physician arbitrarily or without good reason to believe that the physician has information relevant to the case. A subpoena may be served in person a copy left at an office or residence, or served by United States Mail, certified or registered. A subpoena may not be ignored. In most Indiana counties, if it appears to the Court's satisfaction that the person subpoenaed received or was aware of the content of the subpoena, the trial judge will issue a bench warrant to compel a reluctant or disregarding witness' compliance. A bench warrant instructs the county sheriff to find and transport the non-complying witness to appear before the judge. Bench warrants supersede most other types of activity, including professional and social events.

The Trial Rules may require that an attorney request a subpoena be issued to a physician. The physician should not take offense upon receiving a subpoena. The attorney should see to it that the physician has sufficient prior notification and that time schedules are observed where possible.

B. Opposition to Subpoena

The Trial Rules provide that a person subpoenaed may apply to the court with reason why the subpoena should not be honored. Legal reasons may result in the withdrawing or "quashing" of the subpoena. Once issued, a subpoena may be modified only by the court. However the party requesting the issuance of a subpoena can refrain from applying to the court for enforcement, thus effectively modifying the subpoena. Cooperation between the person requesting and the person subpoenaed may obviate the need for the subpoena, or result in a "modification" of its terms.

C. Subpoena Duces Tecum

Subpoena "duces tecum" is Latin for "bring with you". Thus, a subpoena duces tecum compels the person subpoenaed to bring with him documents or tangible things. An unreasonable or oppressive subpoena duces tecum can be modified by the court.

VII. CONFERENCE

Unless authorized by the patient, by court order, or by agreement of counsel, opposing counsel should refrain from calling or contacting an examining or treating physician or opposing counsel's specially-employed physician for the purpose of obtaining a medical opinion on a pending case.

Subject to the foregoing, in many cases a conference between the requesting attorney and the physician-witness is not only desirable, but may result in material benefit to both the attorney and the physician. Conferences should be held at a time and place mutually convenient to the conferees. Conferees should be cognizant of time demands and should be prompt. At a conference, the attorney and physician would expect to discuss any and all questions which the attorney anticipates asking the physician in deposition or court, as well as all aspects of the physician's diagnosis, treatment and prognosis for the patient. It is important that both the attorney and physician be completely candid with each other so that there will be no surprises. It is entirely proper for the attorney to point out the kind of medical evidence he needs to establish his case and the reason for it, but this does not excuse an attorney who attempts to shape the physician's testimony. It must be remembered that any improperly presented medical testimony is almost always a bilateral product and one that is professionally unworthy of both the physician and the attorney. The physician is not an advocate for anyone, but is called on in deposition or court to testify as to the details of his diagnosis, treatment and prognosis of a patient or to express an expert opinion based upon his professional judgment and his own conscience, which must mark the limit of his testimony, including his opinion. (See also the discussion at IX, 1).

VIII. THE PHYSICIAN AND THE TRIAL

A. Subpoenas for Trial

Some attorneys will not subpoena a physician they expect to call as a witness, preferring to make personal arrangements with the physician and relying upon his promise to appear. A physician should not take offense at being served with a subpoena. Attorneys subpoena medical witnesses because:

1. It may be desirable, in a particular case, for the physician to be able to testify, if asked, that he appears in court pursuant to a subpoena; or
2. It may be essential in order to secure a continuance if for any reason the physician fails to appear as required.

Under court rules and statutes in the State of Indiana, an attorney is required to subpoena the physician as a witness if the attorney wishes to make the physician's appearance mandatory.

B. Arrangements For Court Appearance

1. The attorney should make arrangements with the physician regarding the time the physician will be called to testify. The attorney should *always* give the physician as much advance notice as possible of trial dates and *all* continuances.

2. Recognizing the time problems of the medical profession, judges and attorneys should make every effort to avoid unnecessary inconveniences for the physician. Notwithstanding, the physician's testimony may not occur on schedule. The process of law and the time of other individuals must also be respected by the physician.

C. Duty to Testify

1. Our system of justice depends upon being able to require any citizen's attendance at a judicial proceeding and to give testimony regarding the case. There is no question as to the obligation of the physician to respond to a subpoena, just as any other citizen, except where a grave emergency prevents his doing so. The physician assumes the risk, including contempt, of convincing the court that the emergency was of sufficient gravity to justify his ignoring the order of the court.

2. An attending or treating physician possesses special knowledge regarding a patient's care and treatment. When testimony regarding the patient's condition is necessary, the attending or treating physician has knowledge of those facts, is called a "fact witness", and can be compelled to testify concerning those facts, without regard to the physician's customary or usual time charges for such testimony. (See also the discussion at IX, #1)

3. A physician specially employed to review records or examine a patient for the purpose of expressing an educated medical opinion is an expert witness. Usually, he does not possess information developed from a physician-patient relationship and ordinarily can not be compelled to testify without being compensated in accordance with the physician's customary or usual time charges for such testimony. The employing attorney will arrange for the deposition or trial testimony of the expert witness.

4. The attending physician, when appearing as a witness, should normally provide itemized bills for his medical services, and these should be addressed to the patient. Charges for conferences, depositions and testifying in court should be addressed to the attorney and are in addition to statutory witness fees. See Paragraph IX (2).

5. No attorney is justified in abusing or badgering any witness, including a physician. Established rules of evidence give ample opportunity for testing the completeness or credibility of the medical witness and make unnecessary or unjustifiable recourse to any of the above devices on the part of the cross-examining attorney. If he feels aggrieved, the physician should inquire of the person conducting the hearing whether he is required to submit to such treatment.

IX. MEDICAL FEES

1. The Attending Physician and His Charge for Services in Connection with Litigation

It is proper, and not unusual, for an attorney to represent a client on a contingent fee basis. This client may not be in a position to pay for the legal services unless he prevails in the litigation. The medical profession neither has nor seeks any comparable arrangement. It is perfectly proper for a physician to charge a fee for his time. Fees should take into consideration conferences, preparation of reports required or requested, travel costs and witness appearance.

2. The Attorney and His Direct Payment of Medical Fees

By his standard of ethics, an attorney may not acquire a proprietary interest in the cause of action or subject matter of litigation he is conducting for a client. The question frequently arises whether an attorney may advance costs of litigation on behalf of his client. An attorney shall not advance or guarantee financial assistance to his client, except that an attorney may advance or guarantee the expenses of litigation including court costs, expenses of investigation, expenses of medical examination and costs of obtaining and presenting evidence. The attorney has the responsibility of obtaining evidence in both written and oral form. When an attorney requests that a written medical report be prepared, or arranges for oral testimony or conference, the attorney incurs the reasonable expense for the report preparation or testimony time and is responsible for payment thereof. In addition, with the specific concurrence of this client, an attorney may guarantee that a physician's fees for medical management of the client will be paid from any sums awarded the client. A specific understanding should be reached between the attorney and the doctor in each case. The fees should be reasonable and in line with the services rendered.

X. CONCLUSION

Each of the professions has a duty to develop an enlightened and tolerant understanding of the other. The aims of the two professions are essentially parallel in their service to society. The public must be considered first, and it is the public's interest that must be uppermost in all cases. Each profession must remember that individual practitioners vary in capacities and characteristics and that, while law and medicine may be termed sciences, each is an inexact science and such inexactness is, and always will be, accentuated by the human limitations of its practitioners.

CME QUIZ

TO OBTAIN ONE HOUR OF CATEGORY 1 AMA CME CREDIT, answer the following questions by circling the correct answer on the answer sheet below. Complete and clip the application form and mail it to: Indiana University School of Medicine, CME Division, BR 156, 1226 W. Michigan St., Indianapolis 46223.

Electrolyte Disturbances

CONTINUED FROM PAGES 13-19

1. A *chronic* reduction in the serum potassium concentration represents a total body deficit of:
   a) 100-200 mEq
   b) About 500 mEq
   c) 600-1000 mEq
   d) 1200-1500 mEq

2. All of the following statements are true *EXCEPT*:
   a) Acute intracellular shifts of potassium secondary to respiratory or metabolic alkalosis are well tolerated.
   b) Chronic potassium losses, such as hypokalemia secondary to diuretic therapy, are well tolerated.
   c) Acute potassium losses, such as hypokalemia secondary to vomiting and diarrhea, are well tolerated.
   d) The acceptable lower limit of serum potassium concentration for elective surgery is poorly defined.
   e) Even partial repletion of total body potassium stores helps normalize electrophysiology and provides an antidysrhythmic effect against digitalis.

3. The treatment of hyperkalemia includes all of the following *EXCEPT*:
   a) Calcium chloride
   b) Sodium bicarbonate
   c) Mechanical hyperventilation of the lungs
   d) Spironolactone
   e) Glucose-insulin infusion

4. The total serum calcium concentration is *directly* proportional to:
   a) The arterial pH
   b) The serum albumin concentration
   c) Calcitonin release
   d) Alveolar ventilation

5. Intraoperative "citrate intoxication," or the binding of calcium cation to citrate anion during massive blood transfusion, is important in:
   a) Hyperthermic patients
   b) Adult patients
   c) Patients with hepatic insufficiency
   d) Patients with metabolic encephalopathy

6. An important sign of magnesium toxicity in the patient with toxemia of pregnancy is:
   a) Absent deep tendon reflexes
   b) Hyperreflexia
   c) Seizures
   d) Tachycardia
   e) Hypertension

7. Hypernatremia is associated with all of the following *EXCEPT*:
   a) Hypovolemia
   b) Adrenal insufficiency
   c) Fever
   d) Burns
   e) End-stage renal disease

8. Appropriate treatment for *the most common cause* of hyponatremia is:
   a) Sodium restriction
   b) Hypotonic fluid administration
   c) Rapid free water administration
   d) Furosemide
   e) Water restriction

9. The Syndrome of Inappropriate ADH Secretion (SIADH):
   a) Improves with spironolactone administration
   b) Is managed with hypertonic saline infusion
   c) Is caused most frequently by overzealous fluid replacement in the perioperative period
   d) Occurs with acute ethanol intoxication
   e) Is characterized by dilutional hyponatremia and oliguria

DECEMBER CME QUIZ Answers

Following are the answers to the CME quiz that appeared in the December 1986 issue: "Carcinoma of the Prostate," by J.G. Morphis II, M.D., and N.B. Hornback, M.D.

1. b	6. a
2. c	7. c
3. d	8. c
4. c	9. a
5. a	10. c

Answer sheet for Quiz: (Electrolyte Disturbances)

1. a b c d	6. a b c d e
2. a b c d e	7. a b c d e
3. a b c d e	8. a b c d e
4. a b c d	9. a b c d e
5. a b c d	

I wish to apply for one hour of category 1 AMA Continuing Medical Education credit through the I.U. School of Medicine. I have read the article and answered the quiz on the answer sheet above. I understand that my answer sheet will be graded confidentially, at no cost to me, and that notification of my successful completion of the quiz (80% of the questions answered correctly) will be directed to me for my application for the Physician's Recognition Award of the American Medical Association. I also understand that if I do not answer 80% of the questions correctly, I will not be advised of my score but the answers will be published in the next issue of INDIANA MEDICINE.

Name (please print or type)

Address

Identification number (found above your name on mailing label)

Signature

To be eligible for this month's quiz, send your completed, signed application before Feb. 10, 1987 to the address appearing at the top of this page.



AUXILIARY REPORT

Alfrieda Mackel (Mrs. Frederick)
ISMA Auxiliary President 1986-87

Is your spouse a member of the Medical Auxiliary? The Indiana State Medical Association Auxiliary (ISMA-A) helps physicians' spouses to be more effective "partners in health". ISMA-A objectives throughout Indiana emphasize *active* participation on all three levels of our organization: county, state and national. If there is no organized auxiliary in your county, you can still participate on the state and national levels by becoming a member in the member-at-large category.

Physician spouses, we need you! If you are a spouse of a medical student, resident or practicing physician, please consider joining the ISMA-A. In 1987, as always, we are seeking members who are interested, educated about the issues and willing to take an active role in the Medical Auxiliary.

As a nationwide network of physicians' spouses, the Medical Auxiliary has raised millions of dollars for medical education and research and has attempted to improve the health and quality of medical care for those around us through a wide variety of public information programs. The auxiliary augments the physician's role by reaching into areas with public information when physicians cannot. As an auxilian, you can also help to make an impact in the area of health legislation.

Medical student/resident spouses may join the AMA-A for $5.00 and the ISMA-A for $2.00. In Marion County the medical students' spouses even have their own association. Other counties are following suit; some even have sponsorship programs.

With the increasing number of female medical students, residents and physicians, the future formula of membership should contain a fairly high percentage of male members. The new ad hoc appointment to the board to represent male members is Rod Ashley (spouse of Susan J. Rogers, M.D. of Marion). Rod has been very active in the recruitment of other male members. His active participation in the Medical Auxiliary has attracted national attention and has caused the auxiliary to re-evaluate the role of male spouses. As a result of that reevaluation, ISMA-A has worked to accommodate male members more readily and has reexamined and redefined its goals and programs, prejudices and limitations, and traditional thinking about ISMA-A being a "women's organization."

With obvious changes in the demographics of our members and potential members, ISMA-A is ready for a period of substantial growth and maturity as an organization. We need to have the help and support of all medical students', residents' and physicians' spouses, male and female, in order to continue to be a productive organization working to promote and support the practice of medicine.

For more information about the ISMA Auxiliary, please contact Mrs. Robert Wrenn (Ann), state membership chairman, at (812) 334-1876.

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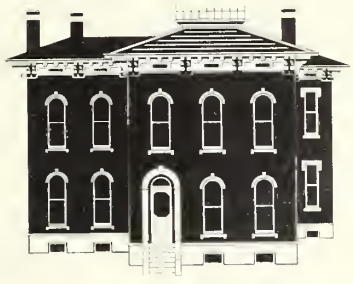
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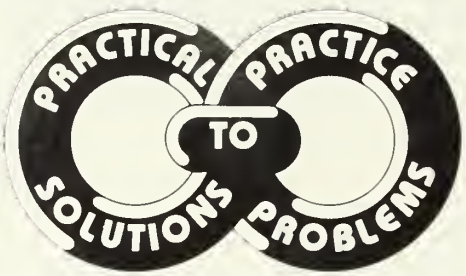
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NEWS NOTES

For the Asking

• **A series of books dealing with computers in medicine** is being published by Springer-Verlag New York, Inc., P.O. Box 2485, Secaucus, N.J. 07094. One such book, *Use and Impact of Computers in Clinical Medicine*, was written by James G. Anderson, Ph.D., Professor of Academic Affairs at Purdue University, and Stephen J. Jay, M.D., Vice-President of Academic Affairs at Methodist Hospital of Indiana. The volume contains about 376 pages and sells for $34.95. A listing of other computer-medicine publications is available from the publisher.

• **"Self-Care and Self-Help Groups for the Elderly: A Directory"** is a publication of the National Institutes on Aging. It provides details about organizations that deal with the concerns of older people or that have programs relevant to older people, their families and health professionals who work with them. The publication is available free of charge from the NIA Information Center/SCSH, 2209 Distribution Circle, Silver Spring, Md. 20910.

• **How Alzheimer's disease progresses** and what physicians can do to ease its impact on patients and their families are discussed in "Alzheimer's Disease: A Clinical Update," a new videocassette with Barry Reisberg, M.D., Associate Professor of Psychiatry of New York University and Clinical Director of the NYU Medical Center's Aging and Dementia Research Program. The video is available in more than 700 hospitals and medical centers through the Network for Continuing Medical Education (NCME).

• **The American Porphyria Foundation** provides primary care physicians with excellent education materials for diagnosis, testing and treatment of each of the porphyrias. For this service and for more information, write to the Foundation at P.O. Box 11163, Montgomery, Alabama 36111.

• **The AMA is offering dramatic anti-smoking posters** and video public service announcements with the message, "Sooner or later everyone quits smoking . . . one way or the other."

• **The American Institute for Cancer Research** has published a booklet that explains the harmful effects of fat. A free copy of "All About Fat and Cancer Risk" may be obtained by sending a SSAE (#10) to the Institute in care of Dept. FC, Washington, D.C. 20069.

• **The CNR Review**, a quarterly newsletter for professionals working with brain-injured persons, is now being published by the Center for Neuropsychological Rehabilitation. To request a copy, contact Lance E. Trexler, Ph.D., Clinical Director, CNR, 8925 N. Meridian St., Suite 100, Indianapolis 46260—(317) 843-8120.

Peer Review Is Called Key to Quality Assurance

Peer review must remain a top priority in the nation's health care facilities if the provision of quality care is to be assured, according to experts speaking at a national forum examining peer review issues.

"In the rapidly changing health care environment, the need for peer review remains constant. It is the basic mechanism for meeting the demands of public accountability and it must be preserved as such," said Dennis S. O'Leary, M.D., president of the Joint Commission on Accreditation of Hospitals, sponsor of the conference which was held in Chicago this fall.

"Quality is a major public policy issue in society today. It is not just an issue for health care practitioners and managers—business, government, insurers and consumers are all deeply interested in quality," O'Leary said. "Peer review is essential to the objective of maintaining a high level of quality patient care."

Among the nationally recognized authorities addressing key aspects of peer review in medicine at the day-long session were Carol McCarthy, Ph.D., president of the American Hospital Association, and James H. Sammons, M.D., executive vice-president of the AMA.

3-Wheel ATVs Targeted by Emergency Physicians

The American College of Emergency Physicians has called for the adoption of regulations aimed at "slowing the epidemic of injuries caused by three-wheel, all-terrain recreation vehicles."

Dr. Michael Ervin, president of the College, wants regulations that would prohibit anyone under 14 from driving the ATVs except under the direct supervision of an adult. He is also calling for the mandatory use of helmets and for the mandatory training, testing and licensing of all ATV operators.

Dr. Ervin cited a recent report by the U.S. Consumer Product Safety Commission that showed children under 12 are unable to operate any size ATV safely and that children under 16 are incapable of operating the larger, adult-sized ATVs safely.

Nurse-Anesthetist Loses Wrongful Discharge Suit

In an action for wrongful discharge, an Indiana appellate court ruled that letters from the executive director of a hospital were not intended to constitute a contract of employment.

A nurse-anesthetist was discharged from her position, which she had held for almost 10 years. In an action against the hospital, she alleged that she and the hospital had entered into an employment contract.

The court found that there was undisputed evidence that the director had told her that only the board of trustees had the authority to enter into contracts with employees.—*Ewing v. Board of Trustees of Pulaski Memorial Hospital*, 486 N.E.2d 1094 (Ind. Ct. of App., Dec. 30, 1985) (Courtesy of *The Citation*, Sept. 15, 1986)

NEWS NOTES

Here and There . . .

Dr. Gregory K. Hindahl of Evansville has been named a diplomate of the American Board of Family Practice.

Dr. Dale D. Dickson of Greensburg, a family physician 53 years, has retired from practice.

Dr. Atanacio H. Tiongson, a Logansport ophthalmologist, has been named a fellow of the American College of Surgeons.

Dr. Joseph D. Richardson of Rochester, president of the Fulton County Diabetes Association, has received the association's annual outstanding volunteer award.

Dr. Jeffrey W. McGuire of Monticello has been named a fellow of the American Academy of Family Physicians.

Dr. Thomas C. Buchanan of Terre Haute has been named a diplomate of the American Board of Orthopaedic Surgery.

Dr. Hugh C. Hendrie, director of the I.U. School of Medicine's Dept. of Psychiatric Research, discussed dementia during a recent Alzheimer's Family Day conference in Muncie.

Dr. John W. Reuter, a Bedford ophthalmologist, discussed glaucoma, cataracts and laser surgery at a recent health forum at the Bedford Medical Center.

Dr. George A. Horvath, a South Bend pediatrician, discussed "Raising Healthy Children" as part of a recent lecture series at the South Bend Clinic; **Dr. David M. Sabato**, an otolaryngologist, discussed issues related to healthy ears and throats.

Dr. Jan R. Reineke and **Dr. Philip DePauw** of South Bend conducted a seminar in November at St. Joseph's Medical Center on "Planning for Pregnancy."

Dr. Alfred A. Serritella of LaPorte was guest speaker at a recent meeting of the local Crohn's/Colitis Support Group.

Dr. Kenneth E. Bobb of Seymour and **Dr. Alfred E. Hollenberg** of Hagerstown have been recognized for 30 years of continuous membership in the American Academy of Family Physicians.

Dr. Kenneth A. Smith, a Fort Wayne rheumatologist, was guest speaker at a recent public forum in Decatur sponsored by the Arthritis Foundation.

Dr. Ned B. Hornback, chairman of the Dept. of Radiation Oncology, I.U. School of Medicine, lectured at Albany Medical College in October on the "Clinical Application of Hyperthermia in Cancer Treatment."



Dr. Feigenbaum

FILE PHOTO

Dr. Harvey Feigenbaum, an I.U. School of Medicine cardiologist, has received a distinguished alumnus award from the I.U. College of Arts and Sciences/Graduate School Alumni Association; he was honored for his major role in developing echocardiography.

Dr. Dennis E. Stone of Columbus discussed health issues related to retirement during a recent public meeting at Bartholomew County Hospital.

Dr. William A. Ringer of Williamsport has been named a fellow of the American Academy of Family Physicians.

Dr. Martin R. See of Indianapolis has been elected to fellowship in the American College of Cardiology.

Dr. John J. Mulcahy, an Indianapolis urologist, was guest speaker at a November meeting of the Indiana Impotence Support Group.

Dr. M. S. Krishna, a Princeton pediatrician, is being featured on a weekly five-minute radio program aired by WRAY; the program, during which topics pertaining to children are discussed, is produced under a grant from Mead Johnson.

Dr. Homayoon Shidnia of the Dept. of Radiation Oncology, I.U. School of Medicine, lectured in Austria and Yugoslavia this fall on thermology and hyperthermia.

Dr. George W. Hicks, an Indianapolis otologist with the Ear Institute of Indiana, has been named to the Governor's Council on Aging.

Dr. Robert D. Arnold, an Indianapolis obstetrician, was recently featured in *The Indianapolis Star* on the occasion of his 16,000th delivery since 1945—an average of about one baby for every day of his medical career.

Dr. Shokri Radpour of Kokomo has been appointed regional chairman, Middle Section, Board of Governors of the American Academy of Otolaryngology-Head and Neck Surgery.

Dr. Robert E. Lega, a Jeffersonville pediatrician, recently spoke to local fourth grade students about the human skeleton, muscle and bone.

Dr. Sheldon J. Friedman of Noblesville was guest speaker at the November luncheon of the Noblesville Chamber of Commerce; he discussed the prevention of heart attacks.

Dr. Elian M. Shepherd of Gary discussed scoliosis during a November program at Methodist Hospitals' Southlake campus.

Dr. Loren E. Jinnings of Auburn, a family physician 57 years, has retired from practice.

Dr. R. Lee Walton, a Marion pediatrician, was guest speaker at a recent meeting of the Marion Area Mothers of Twins Club.

Dr. Dominic J. Moffo of Michigan City discussed osteoporosis during a recent meeting at Memorial Hospital's Women's Resource Center.

Dr. Helen L. Morrison, a Michigan City psychiatrist, talked about how to raise health children during a "Families and Stress" program at Kingwood Hospital where she is director of the Pediatric Psychiatry Center.

Dr. Ada Patricia Harper, an Indianapolis diagnostic radiologist, discussed "Cancer in Women" during the second annual cancer forum at St. John's Medical Center, Anderson; also speaking on cancer topics during the ACS-sponsored meeting were **Drs. Thomas P. Bright, V. C. Amin** and **James E. Currier**, all of Anderson.

Dr. John M. Morse of Terre Haute has been certified in gastroenterology by the American Board of Internal Medicine.

Dr. Schuyler K. Geller of Terre Haute was guest speaker at a November meeting of the local arthritis support group.

Dr. Mark D. Bickers of Floyds Knobs discussed diabetes during a recent public forum at Washington County Memorial Hospital.

Dr. Randolph W. Lievertz, an Indianapolis family physician, recently appeared on the "Indy Today" show on WISH-TV to discuss the delivery of health and medical care for the indigent; on the lecture circuit this fall, he presented talks in Kokomo and Anderson, as well as in Michigan and W. Virginia.

Dr. Malcolm O. Scamahorn will be honored at a 2-5 p.m. reception Sunday, Jan. 18, in the Pittsboro Christian Church Fellowship Hall. He is retiring after 43 years in practice.

ER Physician Says Staff Privileges Were Ended Because of His Criticism

A public hospital was not entitled to summary judgment in an action against it by an emergency room physician who claimed his staff privileges were terminated because he had criticized emergency room conditions at the hospital, a federal appellate court for Indiana has ruled.

The physician was associated with the hospital and was employed by a physicians' group for five years as an ER staff physician. He was given notice of his termination by the physicians' group in April 1983, and the hospital subsequently revoked his staff privileges. He claimed that the physicians' group conspired with the hospital to terminate him because he publicly criticized the emergency room conditions at the hospital. The physicians' group argued that the physician's employment contract provided for termination without cause, and that it acted alone in exercising its right to terminate him. A trial court granted summary judgment in favor of the physicians' group and the hospital, and the physician appealed.

Reversing the decision, the court said that summary judgment was not appropriate. The conduct of officials at the public hospital in allegedly terminating the physician's staff privileges because he publicly criticized emergency room conditions at the hospital constituted state action for purposes of the civil rights statute. A material issue of fact existed as to whether the public hospital and its officials conspired with the physicians' group that employed the physician to terminate his privileges—*Malak v. Associated Physicians, Inc.*, 784 F.2d 277 (C.A.7, Ind., Feb. 24, 1986) (Courtesy of *The Citation*, Sept. 15, 1986)

ISMA's Accreditation Program Wins Official Recognition for 6 Years

The Indiana State Medical Association's CME Accreditation Program has received continued recognition for a period of six years. The approval has been granted by the Committee for Review and Recognition (CRR) of the Accreditation Council for Medical Education (ACCME).

In a letter to Dr. Franklin A. Bryan, chairman of the ISMA Commission on Medical Education, Dr. Howard S. Madigan, CRR chairman, said, "Particularly impressive to the CRR surveyors was the enthusiastic support given to the intrastate accreditation process."

Physician Recognition Awards

The following ISMA physicians are recent recipients of the AMA's Physician Recognition Award. This award is official documentation of Continuing Medical Education hours earned, and is acceptable proof in most states requiring CME in re-registration that the mandatory hours of CME have been accomplished.

Atkins, Steven D., Greenwood
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Daly, Joseph M., Indianapolis
Denny, Forrest L., Indianapolis
Draper, Thomas W., Indianapolis
Hawk, Edgar A., Indianapolis
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Jeevan, Raj, Terre Haute
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Viens, Amarjit, Indianapolis
Weinbaum, Jack G., Terre Haute

NEWS NOTES

Court Says Physician Is Responsible in Early Discharge Case

According to a recent issue of *Medigram*, a weekly newsletter of the Michigan State Medical Society, the California Court of Appeals has reversed a trial court finding of liability against MediCal in the famous case of *Wickline vs. State of California.*

At trial, according to MSMS legal counsel, the state was found liable for injuries resulting from an alleged premature discharge of Mrs. Wickline, which led to the loss of her leg due to post-surgical complications. Her early discharge occurred because the prospective review process of MediCal had refused to extend her admission to the point requested by her treating physician.

In reversing, the appelllate court exonerated the state, finding that, under the circumstances, the ultimate responsibility for the discharge decision was with her treating physician. Importantly, that physician did not pursue avenues of protest against the early discharge ruling of MediCal. The case does not specifically enter a judgment against him because he was not a party at the underlying trial.

Hospital's Peer Review Reports Not Discoverable

Proceedings and reports of a hospital's peer review committees concerning the health care provided to a patient were not subject to discovery by the patient, the Missouri Supreme Court has ruled.

The patient filed a malpractice action against three physicians and a negligence action against the hospital for, among other things, granting staff privileges to the physicians. The patient filed a request to discover incident reports relating to medical services performed by the physicians, peer review committee reports concerning the physicians, documents relating to staff privileges of one of the physicians, and findings of the hospital's credentials committee in granting staff privileges to two of the physicians. A trial court granted a protective order requiring the hospital to produce the documents only to the attorneys and their experts, not to the parties or the public.

On appeal, the court said that the statute prohibiting discovery of peer review committee documents barred the patient from obtaining peer review committee reports. The court said that credentials committee reports were not exempt from discovery unless they specifically concerned health care provided to a patient.

The court said that the hospital's incident reports were subject to discovery by the patient. The hospital argued that they had been prepared in anticipation of litigation and that they were therefore exempt from discovery under the work-product privilege. The court noted that the hospital made no attempt to describe the report or the circumstances under which they were made.—*State of Missouri ex rel. Faith Hospital v. Enright*, 706 S.W.2d 852 (Mo. Sup. Ct., March 25, 1986) (Courtesy of *The Citation*, Oct. 15, 1986)

Hanford Facility Producing Two Radioactive Elements Needed by U.S. Physicians

Two of the radioactive elements that are used by American physicians are being produced on a trial basis in the Fast Flux Test Facility at Westinghouse Hanford. The FFTF was built for experimental use but it has been found that medical isotopes may be produced within the new facility without interfering with the other tests.

The isotopes are Gadolinium-153 and Cobalt-60. Gadolinium-153 is the working ingredient in an advanced bone scanning device that can detect at an early stage and track the progression of osteoporosis. Cobalt-60 is now used for sterilization of medical products and medical equipment and also has potential uses for food irradiation.

Gadolinium-153 results from the irradiation of europium oxide, a rare-earth metal oxide. Cobalt-60 is produced by irradiating cobalt-59.

The isotopes produced at Hanford are distributed by the Isotope Distribution Office at Oak Ridge, Tennessee.

Cancer Investigator Grant Goes to I.U. Professor

Dr. George Weber, professor of pharmacology and toxicology and of experimental oncology and director of the Laboratory for Experimental Oncology at the I.U. School of Medicine, has received an Outstanding Investigator Grant from the National Cancer Institute.

NCI awards these grants to individual investigators who have an outstanding record of discoveries and who have made exceptional progress in developing novel conceptual and experimental approaches in cancer research.

Dr. Weber is internationally known for his work in identifying strategic differences between normal and cancer cells. His accomplishments in biochemistry are equaled by his progress in the pharmacology and experimental therapeutics of neoplastic diseases.

Olympic Academy Plans 5-Day Indianapolis Course

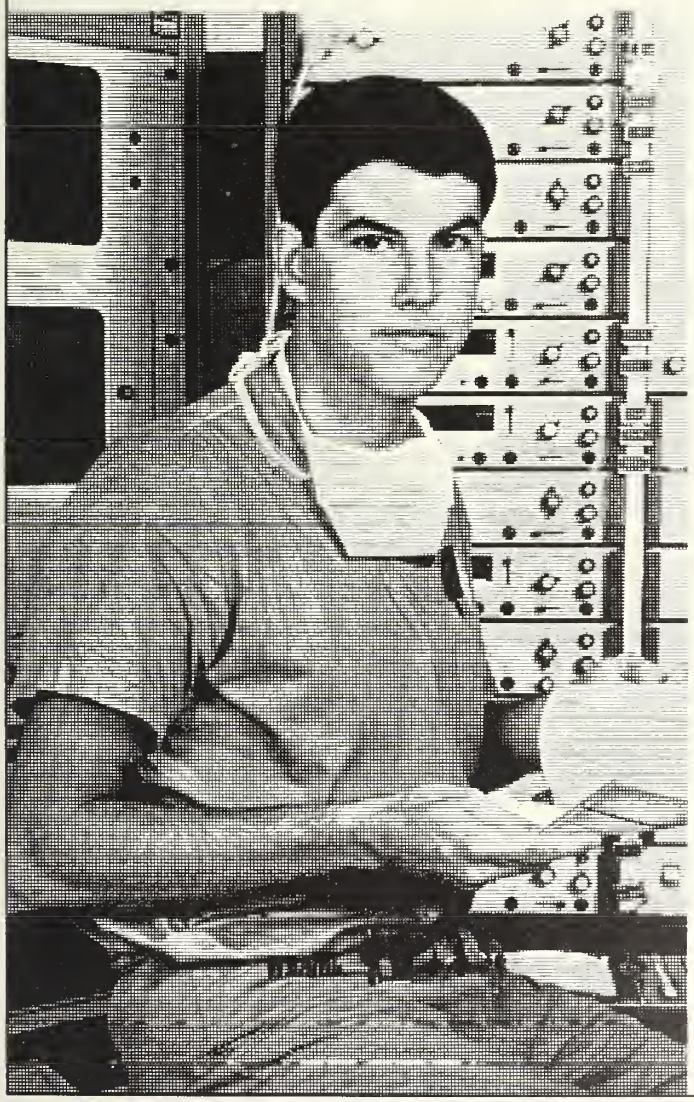
About 350 people are expected to attend U.S. Olympic Academy XI, to be conducted in Indianapolis June 16-20.

The Academy, authorized by the U.S. Olympic Committee, will be hosted in Indianapolis by the IUPUI School of Physical Education, the School of HPER in Bloomington, and the National Institute of Fitness and Sport, Indianapolis.

Listed among the Academy's purposes are to communicate and perpetuate the ideals of the Olympic Games, to explore the values of sport and recreation, and to provide an Olympic Academy program experience to all qualified persons regardless of country of origin, religion, politics or sex.

For information on the Academy, write to Dr. Jeff Vessely, PE 274, School of Physical Education, IUPUI, Indianapolis 46223.

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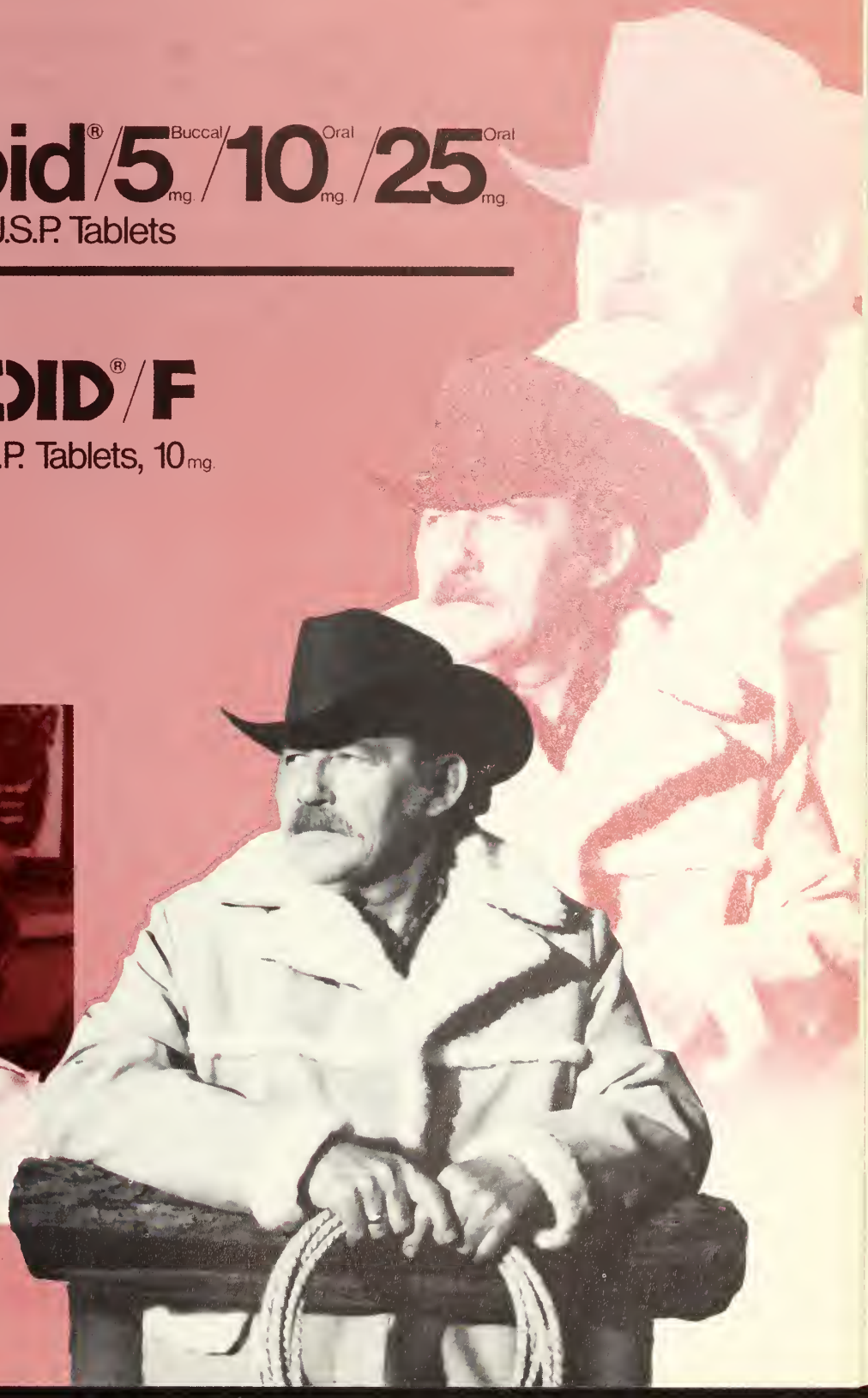
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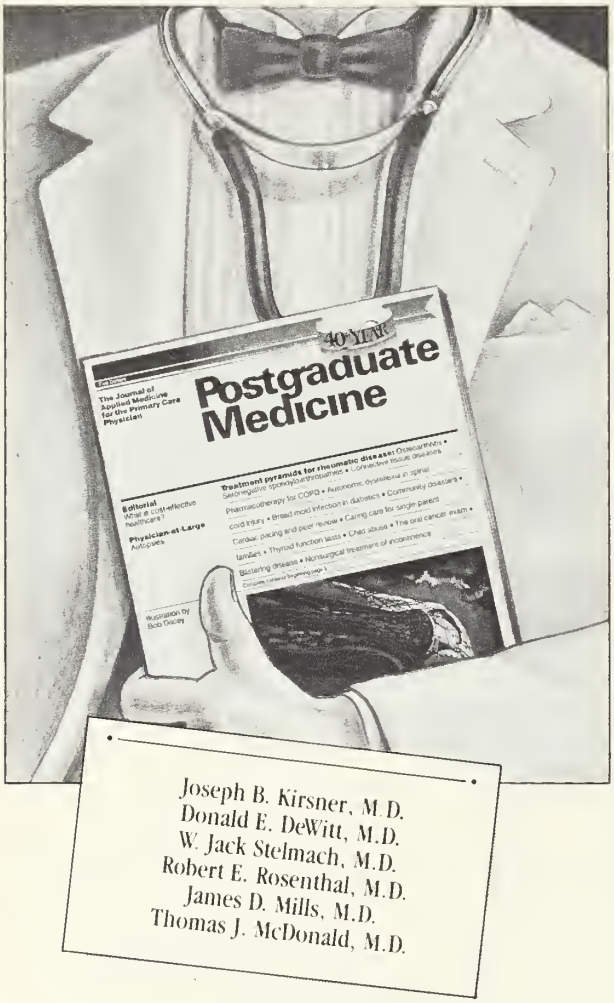
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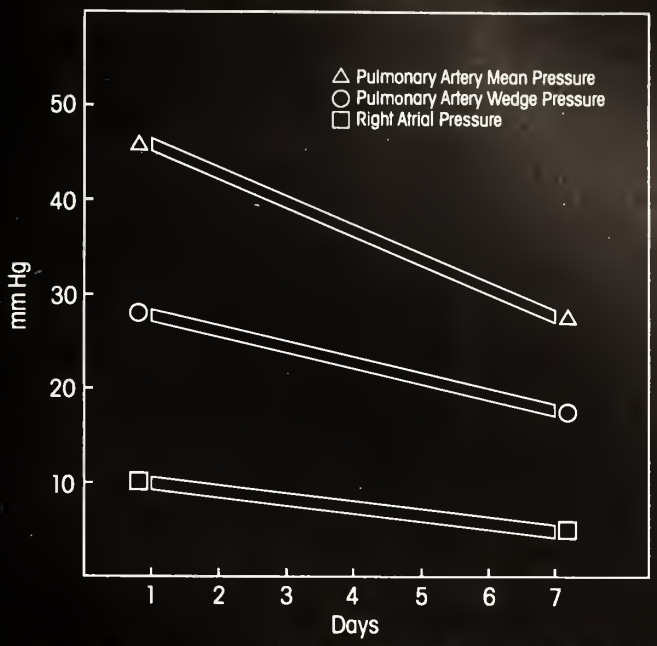
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Almost equal diuretic response occurs after oral and parenteral administration of Bumex. If impaired gastrointestinal absorption is suspected or oral administration is not practical, Bumex should be given by the intramuscular or intravenous route.
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CONTRAINDICATIONS: Anuria. Hypersensitivity and in patients in hepatic coma or in states of severe electrolyte depletion. Although Bumex can be used to induce diuresis in renal insufficiency, any marked increase in blood urea nitrogen or creatinine, or the development of oliguria during therapy of patients with progressive renal disease, is an indication for discontinuation of treatment.
WARNINGS: Dose should be adjusted to patient's needs. Excessive doses or too frequent administration can lead to profound water loss, electrolyte depletion, dehydration, reduction in blood volume and circulatory collapse with the possibility of vascular thrombosis and embolism, particularly in elderly patients.
Prevention of hypokalemia requires particular attention in patients receiving digitalis and diuretics for congestive heart failure, hepatic cirrhosis and ascites, states of aldosterone excess with normal renal function, potassium-losing nephropathy, certain diarrheal states, or other states where hypokalemia is thought to represent particular added risks to the patients.
In patients with hepatic cirrhosis and ascites, sudden alterations of electrolyte balance may precipitate hepatic encephalopathy and coma. Treatment in such patients is best initiated in the hospital with small doses and careful monitoring of the patient's clinical status and electrolyte balance. Supplemental potassium and/or spironolactone may prevent hypokalemia and metabolic alkalosis in these patients.
In cats, dogs and guinea pigs, Bumex has been shown to produce ototoxicity. Since Bumex is about 40 to 60 times as potent as furosemide, it is anticipated that blood levels necessary to produce ototoxicity will rarely be achieved. The potential for ototoxicity increases with intravenous therapy, especially at high doses.
Patients allergic to sulfonamides may show hypersensitivity to Bumex.
PRECAUTIONS: Measure serum potassium periodically and add potassium supplements or potassium-sparing diuretics, if necessary. Periodic determinations of other electrolytes are advised in patients treated with high doses or for prolonged periods, particularly in those on low salt diets.
Hyperuricemia may occur. Reversible elevations of the BUN and creatinine may occur, especially with dehydration and in patients with renal insufficiency. Bumex may increase urinary calcium excretion.
Possibility of effect on glucose metabolism exists. Periodic determinations of blood sugar should be done, particularly in patients with diabetes or suspected latent diabetes.
Patients should be observed regularly for possible occurrence of blood dyscrasias, liver damage or idiosyncratic reactions.
Especially in presence of impaired renal function, use of parenterally administered Bumex should be avoided in patients to whom aminoglycoside antibiotics are also being given, except in life-threatening conditions.
Drugs with nephrotoxic potential and bumetanide should not be administered simultaneously.
Since lithium reduces renal clearance and adds a high risk of lithium toxicity, it should not be given with diuretics.
Probenecid should not be administered concurrently with Bumex.
Concurrent therapy with indomethacin not recommended.
Bumex may potentiate the effects of antihypertensive drugs, necessitating reduction in dosage.
Interaction studies in humans have shown no effect on digoxin blood levels.
Interaction studies in humans have shown Bumex to have no effect on warfarin metabolism or on plasma prothrombin activity.
Pregnancy: Bumex should be given to a pregnant woman only if the potential benefit justifies the potential risk to the fetus.
Bumetanide may be excreted in breast milk.
Pediatric Use: Safety and effectiveness below age 18 not established.
ADVERSE REACTIONS: Muscle cramps, dizziness, hypotension, headache and nausea, and encephalopathy (in patients with preexisting liver disease).
Less frequent clinical adverse reactions are weakness, impaired hearing, rash, pruritus, hives, electrocardiogram changes, abdominal pain, arthritic pain, musculoskeletal pain and vomiting.
Other clinical adverse reactions are vertigo, chest pain, ear discomfort, fatigue, dehydration, sweating, hyperventilation, dry mouth, upset stomach, renal failure, asterixis, itching, nipple tenderness, diarrhea, premature ejaculation and difficulty maintaining an erection.
Laboratory abnormalities reported are hyperuricemia, azotemia, hyperglycemia, increased serum creatinine, hypochloremia, hypokalemia, hyponatremia, and variations in CO_2 content, bicarbonate, phosphorus and calcium. Although manifestations of the pharmacologic action of Bumex, these conditions may become more pronounced by intensive therapy.
Diuresis induced by Bumex may also rarely be accompanied by changes in LDH, total serum bilirubin, serum proteins, SGOT, SGPT, alkaline phosphatase, cholesterol, creatinine clearance, deviations in hemoglobin, prothrombin time, hematocrit, platelet counts and differential counts. Increases in urinary glucose and urinary protein have also been seen.
DOSAGE AND ADMINISTRATION:
Oral Administration: The usual total daily dosage is 0.5 to 2.0 mg and in most patients is given as a single dose.
Parenteral Administration: Administer to patients (IV or IM) with GI absorption problem or who cannot take oral. The usual initial dose is 0.5 to 1 mg given over 1 to 2 minutes. If insufficient response, a second or third dose may be given at 2 to 3 hour intervals up to a maximum of 10 mg a day.
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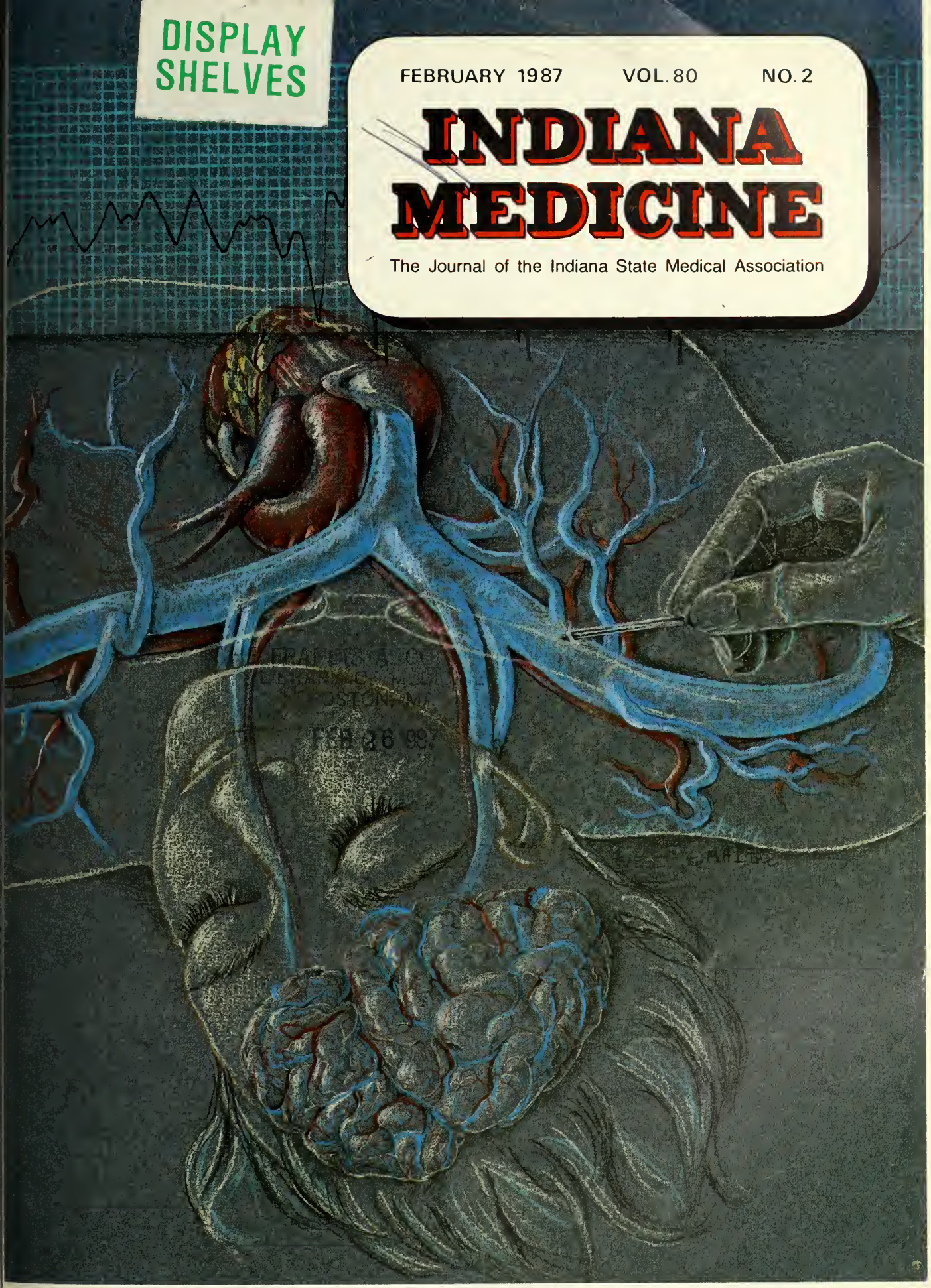
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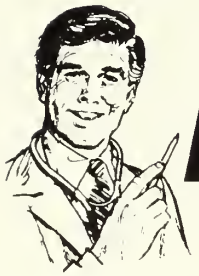
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The Journal of the Indiana State Medical Association



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FEBRUARY 1987

Devoted to the interests of the medical profession and public health in Indiana since 1908.

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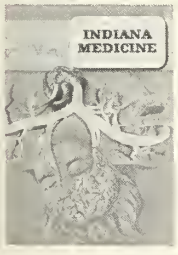
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ABOUT THE COVER

Our series on Critical Care Medicine continues this month with an article by Dr. Michael J. Buran on "Advanced Cardiac Life Support, 1986: The Rationale for New Recommendations."—DRAWING BY BRENDA KESTER, MEDICAL MEDIA PRODUCTIONS, METHODIST HOSPITAL OF INDIANA

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MEDICAL MUSEUM NOTES

CHARLES A. BONSETT, M.D., Indianapolis

THIS MONTH we are back to the subject of radiology and the history of teaching the subject at the Indiana University School of Medicine.

FIGURE 1 you have seen before. It was used as the cover illustration for the March 1984 issue of INDIANA MEDICINE. The photograph shows Dr. Edwin Kime on the right, who at that time (circa 1915) was a medical student, and who later would become chairman of the Department of Anatomy. On the left (identified by a number of readers), is Dr. E. Oscar Lindemuth, who was "Professor of Dermatology and Electrotherapeutics" (and x-ray). The scene, I have been told, is the basement of the Robert Long Hospital, under the front steps.



FIGURE 1

FIGURE 2 is the 1894 graduation photograph of Dr. Albert M. Cole (1870-1928) from the Medical College of Indiana. Dr. Cole, who was born in Charleston, Indiana, received his undergraduate degree from DePauw in 1892. After getting his M.D. degree, he pursued postgraduate study in New York (1895) and in London and Paris (1896-97). His teaching experience commenced in 1899 at the Medical College of Indiana, where he had been appointed as "Assistant to the Chair of Diseases of Children." In 1903 he was appointed "Lecturer in Electrotherapeutics and X-Ray." He was professor by 1908. In 1905 he limited his practice to radiology and, insofar as I have yet determined, was the first Indiana physician to do so. His office was in the Newton Claypool Building, a few blocks away from the medical school.



FIGURE 2

When I.U. united with the proprietary schools in 1908, both Dr. Cole (Medical College of Indiana) and Dr. Lindemuth (State College, i.e., Central College of Physicians and Surgeons) became identified with I.U.S.M. as professors of dermatology and electrotherapeutics.



FIGURE 3



FIGURE 4

FIGURE 3 shows Dr. Lindemuth (1872-1942), who received his undergraduate training from Potts College and Blonnsbury Literary Institute. He was born in Ringtown, Pennsylvania. He received the M.D. degree from the Philadelphia Medico-Chirurgical College in 1906, after which he moved to Indianapolis to practice.

FIGURE 4 shows Dr. Raymond Cole Beeler (1888-1976), a 1912 graduate of I.U.S.M. He commenced practice in 1913 with his maternal uncle, Dr. Albert M. Cole. Dr. Beeler served as radiologist to Base Hospital 32 during World War I and became associated with I.U.S.M in 1919. Following Dr. Beeler's retirement, Dr. John A. Campbell, a 1938 I.U.S.M. graduate, became chairman of the radiology department; he, in turn, was succeeded on his retirement by Dr. Eugene C. Klatte, a 1952 I.U.S.M. graduate.

It is of interest that Dr. Beeler's son, John (I.U.S.M., 1944), and grandson, Richard (I.U.S.M., 1979), are also radiologists.



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WHAT'S NEW?

Acuson has introduced a Fetal M-Mode Software Option to enable obstetricians to gather critical fetal heart data. The software comes under the designation of "Fetal M-Mode Sono-Pac." Acuson also makes the "Cardiology Sono-Pac" ultrasound system, which allows radiologists to provide cardiac imaging services to the cardiology department.

Merck Sharp & Dohme announces a new one-a-day PEPCID (Famotidine MSD), the latest development in H_2 antagonist therapy for active duodenal ulcer and for maintenance therapy of duodenal ulcer after healing. One 40-mg tablet of PEPCID taken at bedtime provides for many patients prompt and lasting pain relief throughout the night and day—with ulcer healing often occurring by week 4.

Norwich Eaton Pharmaceuticals announces that Vivonex® T.E.N. (Total Enteral Nutrition) is now the first elemental (free amino acid) diet that can be prepared for administration without a blender. This significant improvement will lower the risk of contamination, and offer meaningful labor savings throughout the hospital.

Abbott Laboratories has introduced a new assay for the quantitative measurement of 5-hydroxy-3-indole acetic acid (5HIAA) in urine. This amine is useful in diagnosing and monitoring malignant carcinoid syndrome. Some researchers also have reported that 5HIAA is useful as an aid to the diagnosis and management of coeliac disease.

The SON CORPORATION, a national pioneer in fully equipped and furnished modular buildings, recently announced that they are expanding their line to provide Women's Health Care and Breast Evaluation Centers. They are described as energy-efficient, low maintenance buildings ranging from 1,500 to 5,000 square feet. The buildings can be operational in 45 to 60 days. They may be leased, short or long term, with an option to buy.

Happy Rocker has a device that will easily transform a standard wheel chair into a rocker. HAPPY ROCKER™ is a set of channels curved like those on a rocking chair into which the passenger rolls the wheelchair. The front wheels settle into place, the wheelchair brake is set and the rocking begins. Said to be very restful. Non-skid treads and a safety strap are included for the more zealous user.

The VNU New Media Group of Amsterdam, The Netherlands announces MEDDIX DATA, a unique collection of 30,000 slides for diagnosis and training. These illustrations cover a wide spectrum of disciplines of medical and para-medical usage. The material is stored on interactive videodiscs and is easily retrievable. MEDDIX DATA is compatible with IBM Personal Computers.

ICN Pharmaceuticals announces FDA approval for marketing Oxsoralen-Ultra® , a new dosage form of methoxsalen, which can improve the effectiveness of PUVA (psoralen ultraviolet-A) therapy in the treatment of psoriasis. Clinical research shows that patients who required as many as 249 PUVA treatments per year without success now achieve clearing of the disease with as few as 20 treatments annually.

Smith Kline & French has a new packaging for Tagamet. 'Tagamet' 800 mg. Tiltab® in Single Unit Packages are now available. The new packaging contains the recommended dosage for acute ulcer and provides the convenience of once-a-day dosing.

News of what is new in the medical supply industry is composed of abstracts from news releases by book publishers and manufacturers of pharmaceuticals, clinical laboratory supplies, instruments and surgical appliances. Each item is published as news and does not necessarily constitute an endorsement of a product or recommendation for its use by INDIANA MEDICINE or by the Indiana State Medical Association.

Wiley Medical has a new three-volume dictionary, *International Dictionary of Medicine and Biology*. It has produced rave reviews from several clinical and scientific publications. It deals with 150,000 terms, contains 3,200 pages and sells for $395.

Abbott Laboratories has introduced a qualitative enzyme immunoassay that uses a matched combination of monoclonal antibodies to selectively identify human chorionic gonadotropin (hCG) in serum. Known as *TestPack* hCG-serum, the test provides 100% accuracy at 25 mIU/mL and provides results in only four minutes.

Merck Sharp & Dohme is introducing NOROXIN, an important new oral antibacterial agent for patients with urinary tract infections. It offers a spectrum of activity that covers virtually all common uropathogens, including *Pseudomonas* and group D streptococci. Alterations in normal anaerobic bowel or vaginal flora are unusual with NOROXIN, since it is aerobic specific.

Kurt V. Ullman, R.N. of the firm "Medical Communicators" of Carmel will produce newsletters, perform writing and editorial services, and produce office brochures or patient teaching pamphlets for physicians. The newsletters are based on the principle of "doctor talking to patient." Mr. Ullman has a degree in public affairs from I.U. and has five years experience in reporting and editing.

DynaMetric has a phone recorder that is adaptable to "Modular Phones" (the new phones with a small connector on the hand set phone call cord). The recorder makes a clear record of both ends of a conversation a physician has while "on call" or for orders to nurses' stations, prescription pharmacists or for conference calls. It may be used in the office or on the home phone. The record may be reviewed later or transcribed for permanent filing. The device is pocket size and works with standard, mini or micro type cassette recorders.

Acuson has available the Acuson 128 Computed Sonography™ Vascular System. The system includes Doppler and is designed for simultaneous real-time imaging and blood-flow analysis.

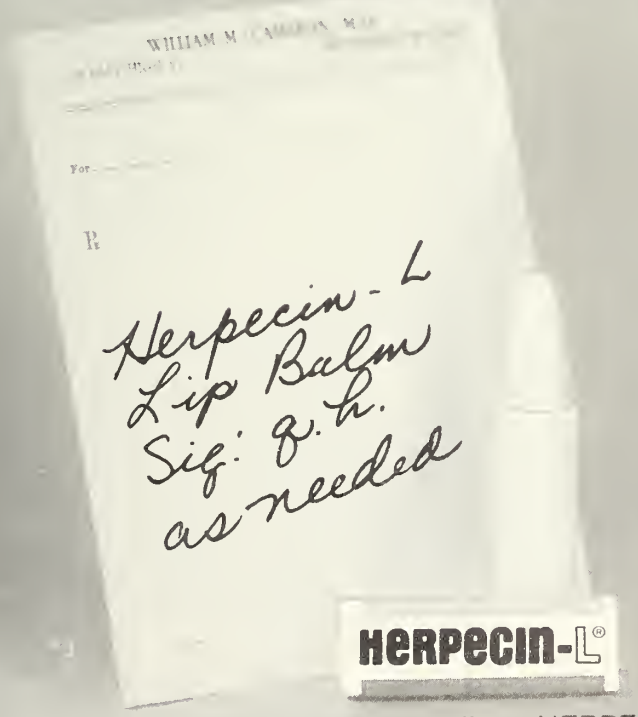
Almost all hypertensives are non-symptomatic. Under the present standard treatment programs, of which there are many variations, most patients develop side effects and feel worse than they did without drugs. This frequent development of troublesone and undesirable side effects often tends to lead to non-compliance, even though the blood pressure has returned to normal levels. The *American Journal of Cardiology* reports that patients receiving calcium channel blockers, together with the non-drug items of hypertensive treatment, have achieved excellent results with no severe side effects. One series reported minor side effects only slightly greater than the adverse reactions to placebo.

Among the more obvious risks usually associated with mistletoe and adults is the idea that ingestion of the berries or leaves by children produces a serious and sometimes fatal reaction. An article in *Annals of Emergency Medicine* reports that children who swallowed one to three berries or leaves had no serious toxicity in any of 14 cases. The FDA received reports of 318 cases between 1978 and 1983. The vast majority showed no toxicity symptoms and there were no deaths.

Mitsubishi Electric has developed a medical image work station capable of displaying and storing the full 2048x2048 line image provided by both x-ray film laser scanners and high resolution digital radiography. In addition to its 2048-line image—the maximum available in the industry—the Mitsubishi 2000 Medical Image Display Station has density resolution of 1,024 "grey levels" for precise display of contrast and brightness.

Raytheon Medical Systems announces the "Spectrum 150 DT" digital nuclear imaging system. It is an integrated product with a gamma camera subsystem and a data processing subsystem. The camera includes not only the camera but the table on which the patient lies, the detector, the electronics that convert the signals from the camera into digital data, and a television monitor whereby the operator communicates with the subsystem. Both camera and patient table move, maintaining field of view and center axis of position during body contouring orbits. The digital image may be manipulated on the screen for sharpness, contrast, magnification and other qualities. Film-saving is considerable since the image is placed on film only after it is at its maximum diagnostic clarity and precision. The term "SPECT" is applied to the imaging process, since the process is described as "single photon emission computerized tomography."

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FUTURE FILE

Medical Malpractice

The American Bar Association National Institute will conduct a program on "Medical Malpractice: Law, Theory and Practice for Attorneys, Physicians and Risk Managers" March 18-20 at the Marriott Hotel, Denver.

For the program and more information, contact the ABA, Division for Professional Education, Dept. N1448, 750 N. Lake Shore Drive, Chicago 60611—(312) 988-6200.

Methodist Hospital CME

April 8: Alternative Care, Sheraton Meridian, Indianapolis.

April 13-15: 7th Annual House Staff Alumni Meeting—"From Lasers to Lithotripsy: Recent Technological Breakthroughs in Surgery"—Hotel Royal Plaza, Lake Buena Vista, Orlando, Fla.

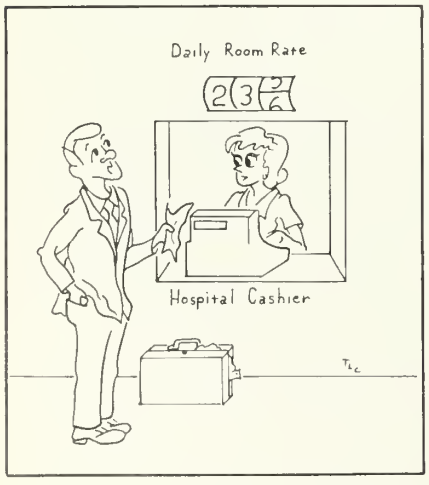
April 29: R.T.P.A. in Acute Myocardial Infarction, Methodist Hospital Auditorium.

May 1: 13th Annual William Niles Wishard Jr. Memorial Lecture, Methodist Hospital, Indianapolis.

May 14-15: 22nd Annual Gordon W. and Mae Batman Lecture Series, Methodist Hospital, Indianapolis.

(February and March courses are listed in the January 1986 issue of INDIANA MEDICINE, page 6.)

For more information, contact Dixie Estridge, CME coordinator, Graduate Medical Center, Methodist Hospital of Indiana—(317) 929-3733.



The *Journal of the American Medical Association* publishes a list of CME courses for the United States twice yearly. The January listing features courses offered from March through August; the July listing features courses offered from September through February.

AMA Marketing Strategies

"Marketing Strategies for Private Practice" is the topic of an AMA practice management workshop to be conducted Friday, March 27, at St. Vincent Hospital, Indianapolis.

The workshop will cover how the basic concepts of modern marketing can be applied to medical practice. For more information on registration of physicians and staff for this eight-hour workshop, please contact Carol Ann Cunningham at ISMA Headquarters.

Evansville Seminars

The Spring Seminars at St. Mary's Medical Center in Evansville will include the MacKenzie Seminar on "Issues in Routine Prenatal and Perinatal Care" on March 12, and the Geriatric Seminar-Part IV on "Sleep and Nutrition in the Elderly" on April 9.

Each program will fall on Thursday and will begin at 1 p.m. For more information, call Dr. W. T. Spain at (812) 479-4468.

2-Day Harvard Course

The Division of Primary Care of Harvard Medical School is offering a course, "The Terminally Ill Patient: Psychological, Social, Legal and Ethical Issues," scheduled for April 24-25 at the Copley Plaza Hotel in Boston. The course will be conducted by Stephen R. Scher, Ph.D., J.D.

For information, contact the Harvard Medical School, Dept. of Continuing Education, Boston 02115—(617) 732-1525.

Blood Pressure Control

"The National Conference on High Blood Pressure Control" will be held April 24-26 at the Tropicana Hotel, Las Vegas. The title of the program is "Consensus Amid Controversy."

Advance registration is $175. For details, contact the National Conference on High Blood Pressure Control, 2121 Wisconsin Ave., N.W., Suite 410, Washington, D.C. 20007—(202) 944-3176.

Indiana University CME

March 18: Dermatology Update for the Non-Dermatologist, Sheraton Marten House, Indianapolis.

March 20: Clinical Aspects of Immunosuppressive Therapy in Multiple Sclerosis, Embassy Suites-Downtown, Indianapolis.

March 20: Management of the School-Aged Hearing Impaired Child, Myers Auditorium, Wishard Memorial Hospital, Indianapolis.

April 4-5: Advanced Trauma Life Support, Tudor Auditorium, Wishard Memorial Hospital, Indianapolis.

April 2-5: Rhinoplasty: Nasal Aesthetic and Reconstructive Surgery, Embassy Suites-Downtown, Indianapolis.

April 6-8: Update Workshop in Echocardiography, Indiana University Medical Center, Indianapolis.

For further information on these and other CME programs, contact Melody Dian, Assistant Director, CME, I.U. School of Medicine—(317) 274-8353.

Oncology Meeting

The spring meeting of the Hoosier Oncology Group will be conducted from 9 a.m. to 3:30 p.m., Saturday, March 21, at Winona Hospital, 3232 N. Meridian St., Indianapolis.

The meeting will feature a presentation by Dr. Eli Glatstein, Chief of Radiotherapy at the National Cancer Institute.

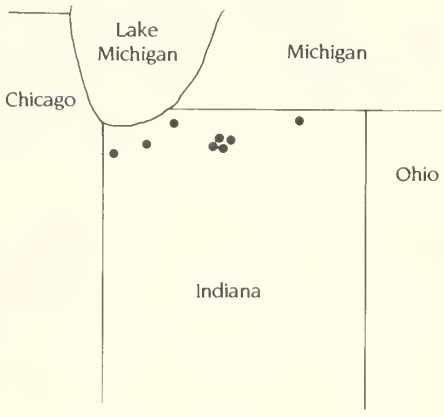
For details, contact Sandra Turner—(317) 927-2115.

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Meridian Healthcare operates eight major facilities in northern Indiana—five of which are clustered in and near St. Joseph's County.

Meridian provides a full range of residence and care options, including The Milton Home—a luxurious lifestyle for fully independent seniors—and The Manor, which offers home-like surroundings for those needing minimal assistance. Meridian Nursing Centers offer both long-term and short-term, or "respite," care. Rehabilitative services, such as physical, speech and occupational therapies are also available.



Meridian has prepared a referral information kit detailing our facilities and services. In it you will find information on how you and your patients' families in the northern Indiana areas served by our eight facilities can take advantage of the many nursing care programs that we offer. This kit is available, without charge, to physicians and hospital administrations. To obtain a copy for your office, please clip and send the coupon below.

Healthcare
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Elkhart, Indiana 46515

Please send me Meridian Healthcare's Physicians' information and referral guide.

Name _____

Address _____

Telephone _____

Organization _____

For hospitals and PA's with need for more than one information kit, please indicate the number of additional kits needed _____.

CANCER CORNER

WILLIAM M. DUGAN, JR., M.D.
Methodist Hospital Cancer Care Center, Indianapolis

CAMP LITTLE RED DOOR, the only camp in Indiana for children with cancer, will host children throughout the state between the ages of 8 and 18 for seven days of canoeing, swimming, arts and crafts, archery and fun. Together, these special children participate in activities that are normal to other children.

The camp is located in the Camp Riley facilities in Bradford Woods, approximately 30 minutes south of Indianapolis. It has paved paths throughout so that wheelchair-bound campers can have the run of the camp. The camp is also fully equipped with medical facilities, and a doctor and nurse from Riley Hospital for Children are on call 24 hours a day for the entire week.

The dates for the 1987 camp are June 14-20. Applications are currently being distributed and can be obtained through the Little Red Door, Marion County Cancer Society, 1801 N. Meridian St., Indianapolis 46202. The cut-off dates for accepting applications will be May 1, 1987.

The cost per camper for one week of overnight camping is $375. The Little Red Door (a United Way Agency) subsidizes this fee and requests that campers pay only $75 to attend. However, if the camper cannot afford the $75 fee, the Little Red Door will provide a campership so that no child is denied attendance for lack of funds.

NEW STRATEGIES IN THE MANAGEMENT OF LUNG CANCER will be the topic of the R. Livingston Ireland Cancer Center's 1987 Major Advance in Oncology series on April 25, 1987. Kenneth Cowan, M.D., Ph.D., from the National Cancer Institute in Bethesda, Md. will present "Drug Resistance in Human Tumors: Recent Developments in New Therapeutic Approaches." Richard Gralla, M.D., from Cornell University Medical College in New York, will present "Management of Non Small Cell Cancer" and Robert B. Livingston, M.D., from the University of Washington in Seattle, will present "Small Cell Lung Cancer: Overcoming an Impass." The one-day conference carries CME credit.

For additional information contact: Barbara Guy, Assistant Director, Ireland Cancer Center, Lowman Building 211, University Hospitals of Cleveland, 2074 Abington Road, Cleveland, Ohio 44106, or phone 216/844-7856.

FACING CANCER addresses patient problems in a positive tone. Six cancer patients share personal experiences with candid statements in regard to accepting diagnosis, learning about the disease and treatments, maintaining open communication and assuming responsibilities. Scott Helt, M.S., an oncology rehabilitation counselor, elaborates on patient comments and emphasizes the importance of maintaining control over life.

A product of the Education and Staff Development at Lincoln General Hospital in Lincoln, Neb., the program is available in 3/4″ videocassette, 1/2″ Betamax and 1/2″ VHS. The purchase price is $250 or you can preview the program for three days at a cost of $50. For further information, contact Education and Staff Development, Lincoln General Hospital, 2300 S. 16th St., Lincoln, Neb. 68502.

THE AMERICAN CANCER SOCIETY IN INDIANA is ready to help when cancer strikes. Most of the American Cancer Society has been through the frightening experience, and through specialized programs of the Society, are ready to help with specific services and support.

There are several programs that can help support the cancer patient, the family and friends. The programs include:

- CANSURMOUNT, a program that provides cancer patients and family an opportunity to share with someone who has experienced cancer, either as a patient or member of a patient's family.
- I CAN COPE, a cancer education course for patients and their families. Through professional lectures and sharing common experiences, participants learn about cancer, coping with daily problems, expressing feelings and other helpful topics.
- ROAD TO RECOVERY, this program includes trained A.C.S. volunteers available to drive cancer patients from home to the nearest treatment facilities at no cost.
- CORPORATE ANGEL NETWORK, an independent program from the A.C.S., which attempts to arrange for private aircraft to transport, at no cost, cancer patients to and from cancer treatment centers.
- FAMILIES FACING CANCER is a series of informal meetings for cancer patients, their families, and those who are faced with caring for cancer patients.
- REACH TO RECOVERY is a program that serves those who have had breast cancer surgery. All of the certified volunteers are rehabilitated mastectomy persons. Services include visitation, guidance, free temporary prosthesis and informative literature for continued rehabilitation.
- LARYNGECTOMY REHABILITATION is a series of meetings that are conducted in cooperation with the International Association of Laryngectomees for persons who have had laryngectomy surgery and their families. Services include visitation, speech therapy, free supplies, and information.
- OSTOMY REHABILITATION consists of certified volunteers who provide visitation and counseling in cooperation with the United Ostomy Association. Free ostomy supplies are available on a short-term basis and informative literature is provided.

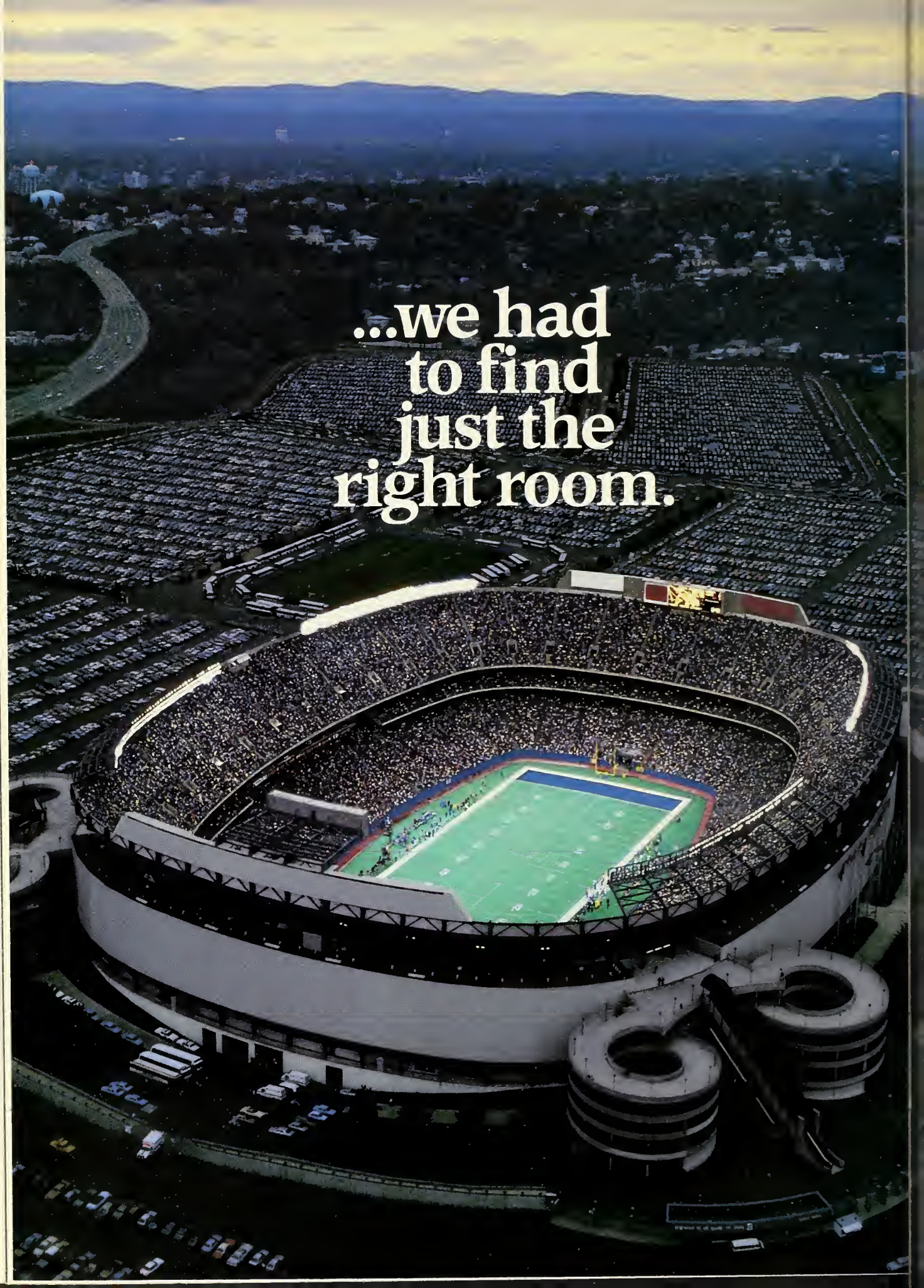
For further information regarding any of these programs, contact your local American Cancer Society office or call the Indiana Division office at 317/872-4432.

To show you how many hypertensives stayed on

INDERAL® LA
(PROPRANOLOL HCl)

after a major nationwide trial...




...we had
to find
just the
right room.

60,073 patients (90%) who started on INDERAL® LA stayed on INDERAL LA.[1*]

Surprising? Not really.

Because most patients on INDERAL LA (propranolol HCl) don't even know it's working.
A recent double-blind, placebo-controlled, crossover study in 138 hypertensive patients[2] revealed that INDERAL LA has a side effects profile unsurpassed by atenolol or metoprolol—which shows how well-tolerated once-daily INDERAL LA can be.

Sole therapy or concomitant therapy? Fifty-nine percent of the time, INDERAL LA stood on its own.

The patients in the nationwide compliance trial were no different from yours. Generally when the antihypertensive regimen is complicated, compliance may become a problem. So, the effectiveness of INDERAL LA as once-daily monotherapy is a big plus. Of the remaining hypertensives in the program, 36% were controlled merely with the addition of a diuretic to INDERAL LA.

For the noncompliant patients in your practice, INDERAL LA may well be the answer.

Almost 20,000 of the patients in the nationwide compliance trial were identified as having been noncompliant with their previous antihypertensive therapy. Their physicians reported that 88% showed improved compliance when placed on once-daily INDERAL LA.

Control, comfort, and compliance

ONCE-DAILY
INDERAL® LA
(PROPRANOLOL HCl)
LONG ACTING CAPSULES

Like conventional INDERAL Tablets, INDERAL LA should not be used in the presence of congestive heart failure, sinus bradycardia, cardiogenic shock, heart block greater than first degree, and bronchial asthma.

*After a 30-day trial with INDERAL LA, physicians reported that 90% of the patients would remain on INDERAL LA.

The one you know best keeps looking better

Please see next page for brief summary of prescribing information

The one you know best keeps looking better

BRIEF SUMMARY *(FOR FULL PRESCRIBING INFORMATION, SEE PACKAGE CIRCULAR.)*

INDERAL® LA brand of propranolol hydrochloride **(Long Acting Capsules)**

DESCRIPTION. Inderal LA is formulated to provide a sustained release of propranolol hydrochloride. Inderal LA is available as 80 mg, 120 mg and 160 mg capsules.

CLINICAL PHARMACOLOGY. INDERAL is a nonselective beta-adrenergic receptor blocking agent possessing no other autonomic nervous system activity. It specifically competes with beta-adrenergic receptor stimulating agents for available receptor sites. When access to beta-receptor sites is blocked by INDERAL, the chronotropic, inotropic, and vasodilator responses to beta adrenergic stimulation are decreased proportionately.

INDERAL LA Capsules (80, 120, and 160 mg) release propranolol HCl at a controlled and predictable rate. Peak blood levels following dosing with INDERAL LA occur at about 6 hours and the apparent plasma half-life is about 10 hours. When measured at steady state over a 24-hour period the areas under the propranolol plasma concentration-time curve (AUCs) for the capsules are approximately 60% to 65% of the AUCs for a comparable divided daily dose of INDERAL tablets. The lower AUCs for the capsules are due to greater hepatic metabolism of propranolol, resulting from the slower rate of absorption of propranolol. Over a twenty-four (24) hour period, blood levels are fairly constant for about twelve (12) hours then decline exponentially.

INDERAL LA should not be considered a simple mg for mg substitute for conventional propranolol and the blood levels achieved do not match (are lower than) those of two to four times daily dosing with the same dose. When changing to INDERAL LA from conventional propranolol, a possible need for retitration upwards should be considered especially to maintain effectiveness at the end of the dosing interval. In most clinical settings, however, such as hypertension or angina where there is little correlation between plasma levels and clinical effect, INDERAL LA has been therapeutically equivalent to the same mg dose of conventional INDERAL as assessed by 24-hour effects on blood pressure and on 24-hour exercise responses of heart rate, systolic pressure and rate pressure product. INDERAL LA can provide effective beta blockade for a 24-hour period.

The mechanism of the antihypertensive effect of INDERAL has not been established. Among the factors that may be involved in contributing to the antihypertensive action are (1) decreased cardiac output, (2) inhibition of renin release by the kidneys, and (3) diminution of tonic sympathetic nerve outflow from vasomotor centers in the brain. Although total peripheral resistance may increase initially, it readjusts to or below the pretreatment level with chronic use. Effects on plasma volume appear to be minor and somewhat variable. INDERAL has been shown to cause a small increase in serum potassium concentration when used in the treatment of hypertensive patients.

In angina pectoris, propranolol generally reduces the oxygen requirement of the heart at any given level of effort by blocking the catecholamine-induced increases in the heart rate, systolic blood pressure, and the velocity and extent of myocardial contraction. Propranolol may increase oxygen requirements by increasing left ventricular fiber length, end diastolic pressure and systolic ejection period. The net physiologic effect of beta-adrenergic blockade is usually advantageous and is manifested during exercise by delayed onset of pain and increased work capacity.

In dosages greater than required for beta blockade, INDERAL also exerts a quinidine-like or anesthetic-like membrane action which affects the cardiac action potential. The significance of the membrane action in the treatment of arrhythmias is uncertain.

The mechanism of the antimigraine effect of propranolol has not been established. Beta-adrenergic receptors have been demonstrated in the pial vessels of the brain.

Beta receptor blockade can be useful in conditions in which, because of pathologic or functional changes, sympathetic activity is detrimental to the patient. But there are also situations in which sympathetic stimulation is vital. For example, in patients with severely damaged hearts, adequate ventricular function is maintained by virtue of sympathetic drive which should be preserved. In the presence of AV block, greater than first degree, beta blockade may prevent the necessary facilitating effect of sympathetic activity on conduction. Beta blockade results in bronchial constriction by interfering with adrenergic bronchodilator activity which should be preserved in patients subject to bronchospasm.

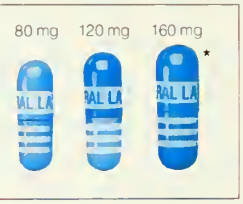
Propranolol is not significantly dialyzable.

ONCE-DAILY

INDERAL® LA

(PROPRANOLOL HCl)

LONG ACTING CAPSULES



INDICATIONS AND USAGE. Hypertension: INDERAL LA is indicated in the management of hypertension, it may be used alone or used in combination with other antihypertensive agents, particularly a thiazide diuretic. INDERAL LA is not indicated in the management of hypertensive emergencies.

Angina Pectoris Due to Coronary Atherosclerosis: INDERAL LA is indicated for the long-term management of patients with angina pectoris.

Migraine: INDERAL LA is indicated for the prophylaxis of common migraine headache. The efficacy of propranolol in the treatment of a migraine attack that has started has not been established and propranolol is not indicated for such use.

Hypertrophic Subaortic Stenosis: INDERAL LA is useful in the management of hypertrophic subaortic stenosis, especially for treatment of exertional or other stress-induced angina, palpitations, and syncope. INDERAL LA also improves exercise performance. The effectiveness of propranolol hydrochloride in this disease appears to be due to a reduction of the elevated outflow pressure gradient which is exacerbated by beta-receptor stimulation. Clinical improvement may be temporary.

CONTRAINDICATIONS. INDERAL is contraindicated in 1) cardiogenic shock, 2) sinus bradycardia and greater than first degree block, 3) bronchial asthma, 4) congestive heart failure (see WARNINGS) unless the failure is secondary to a tachyarrhythmia treatable with INDERAL.

WARNINGS. CARDIAC FAILURE. Sympathetic stimulation may be a vital component supporting circulatory function in patients with congestive heart failure, and its inhibition by beta blockade may precipitate more severe failure. Although beta blockers should be avoided in overt congestive heart failure, if necessary, they can be used with close follow-up in patients with a history of failure who are well compensated and are receiving digitalis and diuretics. Beta-adrenergic blocking agents do not abolish the inotropic action of digitalis on heart muscle.

IN PATIENTS WITHOUT A HISTORY OF HEART FAILURE, continued use of beta blockers can, in some cases, lead to cardiac failure. Therefore, at the first sign or symptom of heart failure, the patient should be digitalized and/or treated with diuretics, and the response observed closely, or INDERAL should be discontinued (gradually, if possible).

IN PATIENTS WITH ANGINA PECTORIS, there have been reports of exacerbation of angina and, in some cases, myocardial infarction, following abrupt discontinuance of INDERAL therapy. Therefore, when discontinuance of INDERAL is planned the dosage should be gradually reduced over at least a few weeks, and the patient should be cautioned against interruption or cessation of therapy without the physician's advice. If INDERAL therapy is interrupted and exacerbation of angina occurs, it usually is advisable to reinstitute INDERAL therapy and take other measures appropriate for the management of unstable angina pectoris. Since coronary artery disease may be unrecognized, it may be prudent to follow the above advice in patients considered at risk of having occult atherosclerotic heart disease who are given propranolol for other indications.

Nonallergic Bronchospasm (e.g., chronic bronchitis, emphysema) — PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD IN GENERAL NOT RECEIVE BETA BLOCKERS. INDERAL should be administered with caution since it may block bronchodilation produced by endogenous and exogenous catecholamine stimulation of beta receptors.

MAJOR SURGERY. The necessity or desirability of withdrawal of beta-blocking therapy prior to major surgery is controversial. It should be noted, however, that the impaired ability of the heart to respond to reflex adrenergic stimuli may augment the risks of general anesthesia and surgical procedures.

INDERAL (propranolol HCl), like other beta blockers, is a competitive inhibitor of beta-receptor agonists and its effects can be reversed by administration of such agents, e.g., dobutamine or isoproterenol. However, such patients may be subject to protracted severe hypotension. Difficulty in starting and maintaining the heartbeat has also been reported with beta blockers.

DIABETES AND HYPOGLYCEMIA. Beta-adrenergic blockade may prevent the appearance of certain premonitory signs and symptoms (pulse rate and pressure changes) of acute hypoglycemia in labile insulin-dependent diabetes. In these patients, it may be more difficult to adjust the dosage of insulin.

THYROTOXICOSIS. Beta blockade may mask certain clinical signs of hyperthyroidism. Therefore, abrupt withdrawal of propranolol may be followed by an exacerbation of symptoms of hyperthyroidism, including thyroid storm. Propranolol does not distort thyroid function tests.

IN PATIENTS WITH WOLFF-PARKINSON-WHITE SYNDROME, several cases have been reported in which, after propranolol, the tachycardia was replaced by a severe bradycardia requiring a demand pacemaker. In one case this resulted after an initial dose of 5 mg propranolol.

PRECAUTIONS. *General.* Propranolol should be used with caution in patients with impaired hepatic or renal function. INDERAL (propranolol HCl) is not indicated for the treatment of hypertensive emergencies.

Beta-adrenoreceptor blockade can cause reduction of intraocular pressure. Patients should be told that INDERAL may interfere with the glaucoma screening test. Withdrawal may lead to return of increased intraocular pressure.

Clinical Laboratory Tests. Elevated blood urea levels in patients with severe heart disease; elevated serum transaminase, alkaline phosphatase, lactate dehydrogenase.

DRUG INTERACTIONS. Patients receiving catecholamine-depleting drugs such as reserpine should be closely observed if INDERAL is administered. The added catecholamine-blocking action may produce an excessive reduction of resting sympathetic nervous activity which may result in hypotension, marked bradycardia, vertigo, syncopal attacks, or orthostatic hypotension.

Carcinogenesis, Mutagenesis, Impairment of Fertility. Long-term studies in animals have been conducted to evaluate toxic effects and carcinogenic potential. In 18-month studies in both rats and mice, employing doses up to 150 mg/kg/day, there was no evidence of significant drug-induced toxicity. There were no drug-related tumorigenic effects at any of the dosage levels. Reproductive studies in animals did not show any impairment of fertility that was attributable to the drug.

Pregnancy. Pregnancy Category C. INDERAL has been shown to be embryotoxic in animal studies at doses about 10 times greater than the maximum recommended human dose.

There are no adequate and well-controlled studies in pregnant women. INDERAL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. INDERAL is excreted in human milk. Caution should be exercised when INDERAL is administered to a nursing woman.

Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS. Most adverse effects have been mild and transient and have rarely required the withdrawal of therapy.

Cardiovascular: bradycardia, congestive heart failure, intensification of AV block, hypotension, paresthesia of hands, thrombocytopenic purpura, arterial insufficiency, usually of the Raynaud type.

Central Nervous System: lightheadedness, mental depression manifested by insomnia, lassitude, weakness, fatigue, reversible mental depression progressing to catatonia; visual disturbances, hallucinations, an acute reversible syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability, slightly clouded sensorium, and decreased performance on neuropsychometrics.

Gastrointestinal: nausea, vomiting, epigastric distress, abdominal cramping, diarrhea, constipation, mesenteric arterial thrombosis, ischemic colitis.

Allergic: pharyngitis and agranulocytosis, erythematous rash, fever combined with aching and sore throat, laryngospasm and respiratory distress.

Respiratory: bronchospasm.

Hematologic: agranulocytosis, nonthrombocytopenic purpura, thrombocytopenic purpura.

Auto-Immune: In extremely rare instances, systemic lupus erythematosus has been reported.

Miscellaneous: alopecia, LE-like reactions, psoriasiform rashes, dry eyes, male impotence, and Peyronie's disease have been reported rarely. Oculomucocutaneous reactions involving the skin, serous membranes and conjunctivae reported for a beta blocker (practolol) have not been associated with propranolol.

DOSAGE AND ADMINISTRATION. INDERAL LA provides propranolol hydrochloride as a sustained-release capsule for administration once daily. If patients are switched from INDERAL tablets to INDERAL LA capsules, care should be taken to assure that the desired therapeutic effect is maintained. INDERAL LA should not be considered a simple mg for mg substitute for INDERAL. INDERAL LA has different kinetics and produces lower blood levels. Retitration may be necessary especially to maintain effectiveness at the end of the 24-hour dosing interval.

HYPERTENSION — *Dosage must be individualized.* The usual initial dosage is 80 mg INDERAL LA once daily, whether used alone or added to a diuretic. The dosage may be increased to 120 mg once daily or higher until adequate blood-pressure control is achieved. The usual maintenance dosage is 120 to 160 mg once daily. In some instances a dosage of 80 mg may be required. The time needed for full hypertensive response to a given dosage is variable and may range from a few days to several weeks.

ANGINA PECTORIS — *Dosage must be individualized.* Starting with 80 mg INDERAL LA once daily, dosage should be gradually increased at three to seven day intervals until optimum response is obtained. Although individual patients may respond at any dosage level, the average optimum dosage appears to be 160 mg once daily. In angina pectoris, the value and safety of dosage exceeding 320 mg per day have not been established.

If treatment is to be discontinued, reduce dosage gradually over a period of a few weeks (see WARNINGS).

MIGRAINE — *Dosage must be individualized.* The initial oral dose is 80 mg INDERAL LA once daily. The usual effective dose range is 160-240 mg once daily. The dosage may be increased gradually to achieve optimum migraine prophylaxis. If a satisfactory response is not obtained within four to six weeks after reaching the maximum dose, INDERAL LA therapy should be discontinued. It may be advisable to withdraw the drug gradually over a period of several weeks.

HYPERTROPHIC SUBAORTIC STENOSIS — 80-160 mg INDERAL LA once daily.

PEDIATRIC DOSAGE — At this time the data on the use of the drug in this age group are too limited to permit adequate directions for use.

*The appearance of these capsules is a registered trademark of Ayerst Laboratories.

REFERENCES:

1. INDERAL LA National Compliance Evaluation Program. Data on file, Ayerst Laboratories.
2. Ravid M, Lang R, Jutrin I. The relative antihypertensive potency of propranolol, oxprenolol, atenolol, and metoprolol given once daily. *Arch Intern Med* 1985;145:1321-1323.

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Advanced Cardiac Life Support, 1986: The Rationale for New Recommendations



ADULT CRITICAL CARE MEDICINE

Methodist Hospital OF INDIANA, INC

MICHAEL J. BURAN, M.D.
Indianapolis

THE RELATIONSHIP between the science of resuscitation and the art of resuscitation has paralleled the course of other areas of medicine. New information becomes available and needs to be rationally introduced into practice. The 1979 National Conference on Cardiopulmonary Resuscitation and Emergency Cardiac Care stated that "meager scientific support for any currently recommended procedure should be noted and recommendations for the development of a more solid data base be made."[1] In this spirit the standards and guidelines for advanced cardiac life support evolved during the 1985 National Conference contain many changes in their recommendations for the care of a patient who has sustained a cardiac arrest.[2]

The major emphasis of cardiopulmonary resuscitation remains the prevention of sudden cardiac death by improving medical therapy for its major predisposing factor, atherosclerotic coronary artery disease. Progress continues in the identification of patients at high risk for life-threatening arrhythmias, as well as the development of a rational approach to prophylactic medical and surgical therapy. In spite of this, sudden cardiac death remains a major public health problem in the mid-1980s. Once cardiac arrest has been identified, the first priorities of therapy remain the rapid application of the ABC's of basic life support followed by definitive therapy (Advanced Cardiac Life Support—or ACLS) to return spontaneous circulation.

Previous standards recommended the delivery of "four big breaths" stacked in a stepwise manner as the initial maneuver in rescue breathing.[1] It is established that the high pressures required to provide these breaths may force the esophagus open, resulting in inflation of the stomach. The air-filled stomach may interfere with ventilation by restricting diaphragmatic movement and may predispose the patient to regurgitation which could interrupt CPR and result in aspiration. Because of this, the new standards recommend two slower breaths, lasting 1 to 1-1/2 seconds, with complete expiration between breaths, both at the beginning of rescue breathing and after each 15 compressions during single-rescuer CPR. During two-rescuer CPR the recommended ratio of chest compressions to breaths remains five-to-one, but a pause in compressions for 1 to 1-1/2 seconds at the time of ventilation is recommended to allow the slower, low pressure breath to be given. Because of these pauses, it is recommended that chest compressions be increased in rate from 60 to 80 per minute for single-rescuer CPR and from 80 to 100 per minute for two-rescuer CPR.

It is now established that the rapidity with which spontaneous circulation can be restored impacts heavily on the outcome of resuscitation. It is recommended that patients with ventricular fibrillation or tachycardia be electrically defibrillated as soon as equipment is available. This should take precedence over even basic life support, particularly in the monitored setting. The new ACLS standards recommend an initial countershock with 200 joules. The lower initial energy level is based on prospective studies demon-

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strating equal efficacy with that achieved with higher energy levels, and a lower incidence of post defibrillation asystole or conduction disturbances.[3] If initial countershock fails, a second shock at 200-300 joules should be delivered immediately. If the patient remains in ventricular fibrillation a third countershock at 360 joules is administered prior to resuming basic life support and beginning drug administration. Rapid sequential countershock is more likely to succeed in defibrillation than remote individual efforts. This is due to decreases in thoracic electrical impedance induced by the previous depolarizations. Decreased impedance results in more effective delivery of defibrillating energy to the heart during subsequent countershocks and increases the probability of successful defibrillation.[4]

The most radical changes in ACLS standards deal with recommendations for drug therapy. Oxygen remains the most essential "drug" in cardiopulmonary resuscitation and should be administered in concentrations near 100% as soon as possible. Likewise, epinephrine continues to be recommended as standard therapy in all patients requiring chest compressions, in doses of 0.5 mg to 1 mg IV every five minutes. The major benefit of epinephrine is related to its vasoconstrictive (alpha receptor) effects on the peripheral circulation, which improves distribution of the limited cardiac output available during closed chest CPR to favor the central nervous system, and increases diastolic blood pressure, which improves coronary blood flow. The better preservation of cerebral blood flow and improvement in myocardial oxygen delivery benefit the two major target organs of any resuscitative attempt.[5]

Recognition of the value of peripheral vasoconstriction in the setting of chest compressions has, in turn, restricted the number of situations in which the use of the vasodilating beta adrenergic agent, isoproterenol, is recommended. Isoproterenol is only recommended for use as a temporizing measure while preparing for transvenous pacemaker insertion in the patient with an intact pulse and compromising bradycardia that is resistant to atropine. Isoproterenol is no longer appropriate therapy for the treatment of asystole or electromechanical dissociation.[2]

Lidocaine is now the sole recommended first line agent for suppression of ventricular arrhythmias in the cardiac arrest setting, and should be given as an IV bolus dose of 1 mg/kg after initial defibrillation attempts. Repeated doses of 0.5 mg/kg every 8-10 minutes to a total of 3 mg/kg are recommended if failure of defibrillation persists. The purpose of lidocaine is to prevent recurrence of ventricular fibrillation after countershock. Once spontaneous circulation has been restored, all patients who have sustained an arrest secondary to ventricular arrhythmias should be placed on a continuous infusion of IV lidocaine at 2-4 mg/minute. Only bolus therapy is recommended during circulatory arrest.

Bretylium tosylate is no longer recommended as a first line agent for ventricular suppression in CPR. This change is based on clinical studies which showed no advantage of bretylium over lidocaine in this setting.[6,7] However, there is animal data indicating that bretylium may have a primary antifibrillatory effect. This raises the possibility that bretylium could potentiate the effect of DC countershock. Presently bretylium is recommended when ventricular fibrillation has recurred or persisted despite repeated countershock and administration of lidocaine. Recommended dosage is 5 mg/kg IV push initially with subsequent 10 mg/kg doses every 15-30 minutes. Attempts at electrical defibrillation must continue during bretylium dosing.

Drug therapy for asystole and electromechanical dissociation has undergone significant revision. Cardiac arrest associated with these arrhythmias continues to have a very poor prognosis with mortality approaching 100%. The standard of therapy for these arrhythmias consists of chest compressions to provide perfusion and ventilation with 100% oxygen to optimize tissue oxygen delivery and carbon dioxide excretion. Epinephrine is administered to direct blood flow to the brain and improve myocardial oxygen delivery with the intent of optimizing cardiac metabolism, resulting in return of effective automaticity and excitation-contraction coupling. The recommended use of sodium bicarbonate and calcium chloride in these settings is now quite limited.

'The Most Radical Changes in ACLS Standards Deal with Recommendations for Drug Therapy'

Calcium ions are known to play a role in excitation-contraction coupling. Early experimental evidence demonstrated that administration of calcium chloride to animals with hyperkalemia-induced asystole resulted in resumption of cardiac activity. This, coupled with anecdotal reports of calcium-induced ionotropy during cardiac surgery, resulted in the widespread use of calcium chloride in cardiac arrest situations.[8] Concerns over demonstrated hypercalcemia in the post-resuscitation period and theoretical information linking mitochondrial calcium accumulation to accelerated cell death caused this practice to be questioned. Recent prospective studies have clearly demonstrated

that calcium chloride is of no benefit in asystole.[9] While the consensus of the literature is that calcium chloride is equally ineffective in the resuscitation of the patient with electromechanical dissociation, a recent prospective study showed increased survival in a subgroup of patients with widened QRS complexes, peaked T-waves or ST segment elevation on electrocardiograms obtained during arrest.[10]

The ACLS standards in 1986 limit the administration of calcium chloride to only patients with asystole or electro-mechanical dissociation in the setting of hyperkalemia, known hypocalcemia, or calcium channel blocking drug administration. While there may be rationale for calcium chloride in a patient with electromechanical dissociation and prolonged ventricular conduction or ischemic electrocardiogram changes, this is not an ACLS recommendation. The recommended dose of calcium chloride is 2-4 mg/kg as a single IV bolus repeated as necessary.

The use of sodium bicarbonate to compensate for the lactic acidosis of hypoperfusion has also recently been called into question. The last revision of ACLS standards had recommended less sodium bicarbonate use during resuscitation because of documented "overdosing" when the previous empiric recommendations were followed. This often resulted in severe metabolic alkalosis and hypernatremia in the post-arrest period. Severe metabolic alkalosis after resuscitation is associated with decreased hospital survival.[11] Standards in 1980 recommended that sodium bicarbonate be used based on measured arterial blood gases as much as possible, and empiric use be limited to prolonged or unwitnessed arrests.[1]

Recent information has even questioned the scientific rationale for using sodium bicarbonate to correct metabolic acidosis in the cardiac arrest setting. Much of the rapid buffering ability of bicarbonate rests in its ability to combine with hydrogen ion to form carbon dioxide and water. Because cell membranes are freely permeable to carbon dioxide there is a possibility that the carbon dioxide thus produced could diffuse into cells and cause significant intracellular "respiratory" acidosis. Because adequately ventilated lungs are very efficient at carbon dioxide excretion, this tissue respiratory acidosis might not be reflected in arterial blood gases. A large discrepancy in pH and PCO_2 between mixed venous and arterial blood gases has been reported in a group of cardiac arrest patients,[12] and mortality in animal models correlates better with mixed venous hypercapnia and acidosis than with arterial blood gas values.[13] While a prospective study on the benefits of sodium bicarbonate therapy has not been performed, this information reinforces the need for caution in the administration of this drug.

The new ACLS standards recommend use of sodium bicarbonate primarily in patients with known preexisting acidosis with or without hyperkalemia. Sodium bicarbonate should not be administered routinely, and empiric use considered only where the patient has demonstrated resistance to basic life support, intubation and ventilation with 100% oxygen, epinephrine, defibrillation, and antiarrhythmic drug therapy. If sodium bicarbonate is to be administered at all then the dosage should be limited to 1.0 meq/kg initially with subsequent dosages of 0.5 meq/kg every 10 minutes.

Atropine sulfate continues to be recommended in asystole and pulseless bradycardia. A recent restrospective study has shown increased short-term survival when atropine is given to patients with asystole refractory to basic life support, epinephrine and sodium bicarbonate.[14] In this setting, 1.0 mg is given and repeated in five minutes if arrest persists.

The appropriate route of drug administration in a cardiac arrest setting remains uncertain. While the antecubital vein is still the site of choice for venous cannulation during arrest, evidence favors a more rapid onset of action when drugs are administered through a central vein above the diaphragm.[15] Use of central catheterization is thus recommended if circulation cannot be restored after initial peripheral drug administration. Endotracheal administration of epinephrine, lidocaine and atropine remains an alternative in the intubated patient. Intracardiac injection should be used only when no alternative route exists.

The efficacy of temporary pacing in the cardiac arrest setting has yet to be well established. Transvenous and transthoracic pacing catheter insertion in the cardiac arrest setting is ineffective and interferes with other resuscitative efforts. The development of noninvasive transcutaneous pacing offers an alternative to these methods but has not been demonstrated to increase survival in the setting of brady-asystolic arrest.[16] If pacing is used it must be in the setting of ongoing standard advanced cardiac life support.

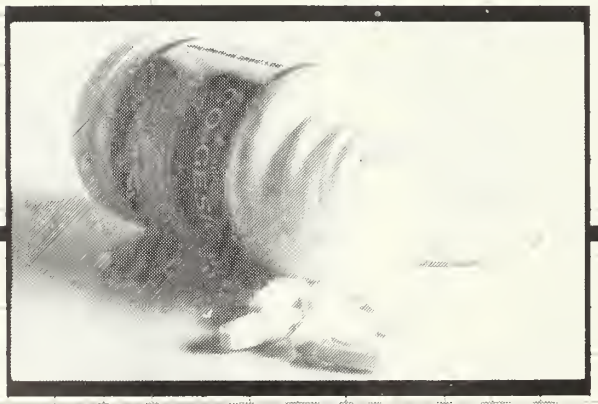
As the science of resuscitation continues to grow, new knowledge is being developed as a result of ongoing investigations. In the future, new information regarding the mechanisms of blood flow during cardiopulmonary resuscitation may greatly alter the way basic life support is provided. Further knowledge of cellular events during profound hypoperfusion may result in important alterations in drug therapy during cardiac arrest. Studies are being developed to investigate the feasibility of immediate femoral-femoral cardiopulmonary bypass for the treatment of refractory asystole or electromechanical dissociation. There is ongoing investigation of the use of drugs such as the calcium channel blockers for preservation of the central nervous system that has been injured by anoxia and hypoperfusion. The results of these and other investigations will guide the development of ACLS standards and the future clinical practice of cardiopulmonary resuscitation.

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METHADONE: Pluses and Minuses

NEIL E. IRICK, M.D.
Indianapolis

THE CONTROL OF chronic pain in the terminally ill patient has become an issue in the provision of hospice care in the United States. The cancer unit of the World Health Organization estimates that 25% of all cancer patients in the world die without relief from severe pain.

Our efforts as physicians are guided by our desire to help alleviate pain and the suffering associated with it. Most of us feel uncomfortably dependent on subjective criteria for determining the efficacy of our efforts. Foley accurately states that "the patient and physician are best served if the physician believes the patient's report."[1]

A random review of 12 charts on our hospice unit revealed that five of those 12 patients were on methadone. Well documented in the nurses' notes was the presence of signs of toxicity in three of those five patients.

The manufacturer's recommended dosage of methadone is 2.5-10 mg every three to four hours. These are dosage ranges needed for the control of pain when the patient regimen is initiated. There is an accumulating body of evidence to prove that these dosages can be excessive for chronic administration. Methadone is an interesting drug in that it has a primary phase half-life and a secondary phase half-life. The former is about 14 hours, which would make it seem like an ideal drug for those patients with chronic pain. However, the secondary phase half-life averages 54.8 hours and can be as long as 97 hours!

If one were to follow the manufacturer's suggested dosages and escalate the dose within two days, very high plasma levels of the drug can accumulate and produce clinical problems. Confusion, agitation, respiratory depression, and even coma can occur with dosages well within the recommended range. We have noted that our older patients frequently report *more* pain as one of the earlier manifestations of clinical accumulation and toxicity. One of the persistent problems with methadone is that there is no correlation between plasma levels and the level of clinical toxicity.

It must be remembered that, because of the extremely long half-life of the drug, changes in the regimen should not be made more than every four to five days, giving considerable disadvantage in dosage flexibility.

One of the problems we face in the treatment of methadone accumulation is the fact that most of the patients have been on some form of narcotic for chronic pain associated with the underlying disease. Treatment of methadone accumulation with naloxone may produce the withdrawal syndrome if naloxone is administered too rapidly. What is often not considered in the treatment of methadone accumulation is that the patient will still be at risk for hours to days because of the secondary phase half-life. A case reported by Ettinger gives more light to this.

A 21-year-old man with widespread bone and lung metastases from a Ewing's sarcoma developed severe respiratory depression and stupor while receiving modified Brompton's mixture containing 20 mg of methadone per dose. Initial dosage of 10 mg per dose had been inadequate, and the dosage had gradually been increased to 20 mg every four hours over a period of one week. The patient's response to naloxone was normal—a reversal of the respiratory depression and a heightened level of consciousness. "Subsequent doses of methadone and cocaine were withheld. Two and one-half hours after the naloxone administration, the patient died of a cardiorespiratory arrest."[2]

Symonds reported the case of an 81-year-old woman who developed respiratory depression after being given 5 mg of methadone three times a day for two days. The patient responded in the expected fashion, but Symonds expressed surprise when informed by the Newcastle Poisons Bureau that the half-life of the drug is 18 to 97 hours.[3]

M.B., an 83-year-old woman admitted to our unit with pain control difficulties, was on methadone at the time of admission. It was decided to continue the same regimen since the patient had been on methadone for less than 48 hours prior to admission.

Over the course of three days, the patient became progressively more sedated. The initial dosage of methadone had been adequate for the patient, but it was obvious from the assessments done by the nursing staff that accumulation of the drug was producing sedation and, finally, unresponsiveness. Cessation of the methadone and institution of morphine in adequate doses to control her pain resulted in the patient regaining her ability to ambulate and care for herself in her own home once again.

J.M., a 67-year-old man admitted for control of pain resulting from metastatic colon carcinoma without serious change in liver function, was initially given 5 mg of methadone every eight hours by the attending physician.

Dr. Irick is Medical Director of the Hospice Program, Methodist Hospital of Indiana, 1701 N. Senate Blvd., Indianapolis, Ind. 46202.

When pain control, on the following day, was judged to be inadequate, the interval between doses was shortened to six hours.

As the patient became disoriented and combative, the dosage was increased to 10 mg. There was only worsening of the disorientation, and the patient tried to escape from the unit twice, using an IV pole as an offensive/defensive weapon.

The patient was given oral haloperidol for control of the acute symtomatology, because of concomitant hypotension. The methadone was discontinued and replaced by long-acting morphine sulfate tablets. The patient experienced a return to normal functioning and thought process over a four-day period. The haloperidol dosage was decreased over the same period of time, but was not discontinued, because of the possible potentiation of the morphine effect on the patient's pain.

Each of these cases summarizes a particular difficulty with the use of methadone in the terminally ill patient.

Currently, the best guidelines to follow in the use of methadone are those of Twycross. He feels that methadone is the strong narcotic of choice for children, but should be avoided in: 1) the elderly or demented; 2) those with confusional symptoms; 3) the presence of elevated intracranial pressure; and 4) those with respiratory, hepatic or renal insufficiency.[4]

Patients who are suffering from methadone accumulation to the point of respiratory depression pose an obvious special problem to the clinician. The most helpful information to date is that of Bradberry and Raebel.[5] Their guidelines for continuous naloxone infusion, as modified by Citron, are as follows:

1) **Preparation of infusion:** Mix three 1 ml ampules (containing 0.4 mg each of naloxone) in normal saline to make a total of 50 ml of solution.

2) **Delivery:** An infusion pump must be used to ensure consistent dosing.

3) **Dosing:** After a bolus of 5 micrograms/kg, begin an infusion immediately at a rate of 2.5 micrograms/kg/hr.[6]

The dosing of naloxone should be titrated to attain the optimal degree of narcotic reversal without precipitating withdrawal symptoms. The infusion should be continued for the duration of the expected half-life of the drug. The patient should be monitored closely for the first 24 hours after the discontinuation of the infusion.

Alternatives to the use of methadone are now beginning to be marketed, although the cost of the medications may be a difficulty for some patients. Long-acting preparations of morphine sulfate are now marketed by two pharmaceutical companies. These are wax-matrix tablets that have the advantage of being a preparation that cannot be altered for intravenous use by addicts.

Newer methods of delivery using syringe drivers and the subcutaneous route are now being used for morphine, hydromorphone and levorphanol. These allow portable infusion in the patient while allowing complete activity with the syringe driver contained in a harness worn by the patient. Patient-controlled portable systems are now available, although the cost of these may be prohibitive of widespread utilization.

Newer applications of common medications in treating the chronic pain of the terminally ill are rapidly achieving acceptance. The use of nonsteroidal anti-inflammatory medications, along with major tranquilizers, antihypertensives, corticosteroids, and tricyclic antidepressants, is becoming common practice as a way of appropriately treating particular aspects of chronic pain that have escaped attention in the past.

Methadone is obviously an excellent drug for the management of chronic pain in the terminally ill patient. The major problems arise from our inability to predict the clinical response, or to monitor the response in relation to blood levels of the drug. The use of methadone requires a great amount of skill. One cannot safely assume that adequate control of chronic pain in the terminally ill patient consists only in giving enough methadone.

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(In controlled studies, recurrences were totally prevented for 4 to 6 months in up to 75% of patients.)

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ZOVIRAX® (acyclovir) CAPSULES

Help free your patients from recurrences.

Daily therapy

Coping with genital herpes is rarely easy. For some, the worst part is the pain and discomfort of frequent attacks—month after month, year after year. For others, the emotional burden presents a more difficult problem, leading to social isolation, anxiety, and diminished self-esteem.

Prevent or reduce recurrences

Although your patients have to live with herpes, they shouldn't have to suffer. Daily therapy with ZOVIRAX CAPSULES can help free them from the cycle of recurrent genital herpes. For many, one capsule three times a day can suppress recurrences completely while on therapy.

Generally well tolerated

Daily therapy with ZOVIRAX CAPSULES is generally well tolerated. The most frequent adverse reactions reported during clinical trials were headache, diarrhea, nausea/vomiting, vertigo, and arthralgia.

The physical and emotional difficulties posed by genital herpes are unique for each patient. The frequency and severity of recurrent episodes as well as the emotional impact of the disease, should be considered when selecting daily therapy with ZOVIRAX CAPSULES.

Please see brief summary of prescribing information on next pag



Prevent recurrences month after month*

ZOVIRAX®

acyclovir)

CAPSULES

rief Summary

NDICATIONS AND USAGE: Zovirax Capules are indicated for the treatment of initial isodes and the management of recurrent epiodes of genital herpes in certain patients.

The severity of disease is variable depending pon the immune status of the patient, the freuency and duration of episodes, and the degree f cutaneous or systemic involvement. These ictors should determine patient management, hich may include symptomatic support and ounseling only, or the institution of specific herapy. The physical, emotional and psychoocial difficulties posed by herpes infections as ell as the degree of debilitation, particularly in nmunocompromised patients, are unique for ach patient, and the physician should deterine therapeutic alternatives based on his or er understanding of the individual patient's eeds. Thus Zovirax Capsules are not appropriate in treating all genital herpes infections. The llowing guidelines may be useful in weighing he benefit/risk considerations in specific disease ategories:

'irst Episodes (primary and nonprimary infections — commonly known as initial genital erpes):

Double-blind, placebo-controlled studies have emonstrated that orally administered Zovirax ignificantly reduced the duration of acute infeion (detection of virus in lesions by tissue culure) and lesion healing. The duration of pain nd new lesion formation was decreased in ome patient groups. The promptness of nitiation of therapy and/or the patient's prior xposure to Herpes simplex virus may influence he degree of benefit from therapy. Patients with nild disease may derive less benefit than those vith more severe episodes. In patients with exremely severe episodes, in which prostration, entral nervous system involvement, urinary etention or inability to take oral medication require hospitalization and more aggressive management, therapy may be best initiated with ntravenous Zovirax.

Recurrent Episodes:

Double-blind, placebo-controlled studies in atients with frequent recurrences (6 or more pisodes per year) have shown that Zovirax apsules given for 4 to 6 months prevented or educed the frequency and/or severity of recurences in greater than 95% of patients. Clinical ecurrences were prevented in 40 to 75% of paients. Some patients experienced increased everity of the first episode following cessation f therapy; the severity of subsequent episodes nd the effect on the natural history of the isease are still under study.

The safety and efficacy of orally administered cyclovir in the suppression of frequent episodes f genital herpes have been established only for p to 6 months. Chronic suppressive therapy is ost appropriate when, in the judgement of the hysician, the benefits of such a regimen outeigh known or potential adverse effects. In eneral, Zovirax Capsules should not be used for he suppression of recurrent disease in mildly ffected patients. Unanswered questions conerning the human relevance of *in vitro* mutagenicity studies and reproductive toxicity studies in animals given very high doses of acyclovir for short periods (see Carcinogenesis, Mutagenesis, Impairment of Fertility) should be borne in mind when designing long-term management for individual patients. Discussion of these issues with patients will provide them the opportunity to weigh the potential for toxicity against the severity of their disease. Thus, this regimen should be considered only for appropriate patients and only for six months until the results of ongoing studies allow a more precise evaluation of the benefit/risk assessment of prolonged therapy.

Limited studies have shown that there are certain patients for whom intermittent short-term treatment of recurrent episodes is effective. This approach may be more appropriate than a suppressive regimen in patients with infrequent recurrences.

Immunocompromised patients with recurrent herpes infections can be treated with either intermittent or chronic suppressive therapy. Clinically significant resistance, although rare, is more likely to be seen with prolonged or repeated therapy in severely immunocompromised patients with active lesions.

CONTRAINDICATIONS: Zovirax Capsules are contraindicated for patients who develop hypersensitivity or intolerance to the components of the formulation.

WARNINGS: Zovirax Capsules are intended for oral ingestion only.

PRECAUTIONS: General: Zovirax has caused decreased spermatogenesis at high doses in some animals and mutagenesis in some acute studies at high concentrations of drug (see PRECAUTIONS — Carcinogenesis, Mutagenesis, Impairment of Fertility). The recommended dosage and length of treatment should not be exceeded (see DOSAGE AND ADMINISTRATION).

Exposure of Herpes simplex isolates to acyclovir *in vitro* can lead to the emergence of less sensitive viruses. The possibility of the appearance of less sensitive viruses in man must be borne in mind when treating patients. The relationship between the *in vitro* sensitivity of Herpes simplex virus to acyclovir and clinical response to therapy has yet to be established.

Because of the possibility that less sensitive virus may be selected in patients who are receiving acyclovir, all patients should be advised to take particular care to avoid potential transmission of virus if active lesions are present while they are on therapy. In severely immunocompromised patients, the physician should be aware that prolonged or repeated courses of acyclovir may result in selection of resistant viruses which may not fully respond to continued acyclovir therapy.

Drug Interactions: Co-administration of probenecid with intravenous acyclovir has been shown to increase the mean half-life and the area under the concentration-time curve. Urinary excretion and renal clearance were correspondingly reduced.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Acyclovir was tested in lifetime bioassays in rats and mice at single daily doses of 50, 150 and 450 mg/kg given by gavage. There was no statistically significant difference in the incidence of tumors between treated and control animals, nor did acyclovir shorten the latency of tumors. In 2 *in vitro* cell transformation assays, used to provide preliminary assessment of potential oncogenicity in advance of these more definitive life-time bioassays in rodents, conflicting results were obtained. Acyclovir was positive at the highest dose used in one system and the resulting morphologically transformed cells formed tumors when inoculated into immunosuppressed, syngeneic, weanling mice. Acyclovir was negative in another transformation system considered less sensitive.

In acute studies, there was an increase, not statistically significant, in the incidence of chromosomal damage at maximum tolerated parenteral doses of 100 mg/kg acyclovir in rats but not Chinese hamsters; higher doses of 500 and 1000 mg/kg were clastogenic in Chinese hamsters. In addition, no activity was found after 5 days dosing in a dominant lethal study in mice. In 6 of 11 microbial and mammalian cell assays, no evidence of mutagenicity was observed. At 3 loci in a Chinese hamster ovary cell line, the results were inconclusive. In 2 mammalian cell assays (human lymphocytes and L5178Y mouse lymphoma cells *in vitro*), positive responses for mutagenicity and chromosomal damage occurred, but only at concentrations at least 400 times the acyclovir plasma levels achieved in man.

Acyclovir has not been shown to impair fertility or reproduction in mice (450 mg/kg/day, p.o.) or in rats (25 mg/kg/day, s.c.). At 50 mg/kg/day s.c. in the rat, there was a statistically significant increase in post-implantation loss, but no concomitant decrease in litter size. In female rabbits treated subcutaneously with acyclovir subsequent to mating, there was a statistically significant decrease in implantation efficiency but no concomitant decrease in litter size at a dose of 50 mg/kg/day. No effect upon implantation efficiency was observed when the same dose was administered intravenously. In a rat peri- and postnatal study at 50 mg/kg/day s.c., there was a statistically significant decrease in the group mean numbers of corpora lutea, total implantation sites and live fetuses in the F_1 generation. Although not statistically significant, there was also a dose related decrease in group mean numbers of live fetuses and implantation sites at 12.5 mg/kg/day and 25 mg/kg/day, s.c. The intravenous administration of 100 mg/kg/day, a dose known to cause obstructive nephropathy in rabbits, caused a significant increase in fetal resorptions and a corresponding decrease in litter size. However, at a maximum tolerated intravenous dose of 50 mg/kg/day in rabbits, there were no drug-related reproductive effects.

Intraperitoneal doses of 320 or 80 mg/kg/day acyclovir given to rats for 1 and 6 months, respectively, caused testicular atrophy. Testicular atrophy was persistent through the 4-week postdose recovery phase after 320 mg/kg/day; some evidence of recovery of sperm production was evident 30 days postdose. Intravenous doses of 100 and 200 mg/kg/day acyclovir given to dogs for 31 days caused aspermatogenesis. Testicles were normal in dogs given 50 mg/kg/day, i.v. for one month.

Pregnancy: ***Teratogenic Effects:*** Pregnancy Category C. Acyclovir was not teratogenic in the mouse (450 mg/kg/day, p.o.), rat (50 mg/kg/day, s.c.) or rabbit (50 mg/kg/day, s.c. and i.v.). There are no adequate and well-controlled studies in pregnant women. Acyclovir should not be used during pregnancy unless the potential benefit justifies the potential risk to the fetus. Although acyclovir was not teratogenic in animal studies,. the drug's potential for causing chromosome breaks at high concentration should be taken into consideration in making this determination.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Zovirax is administered to a nursing woman. In nursing mothers, consideration should be given to not using acyclovir treatment or discontinuing breastfeeding.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS — Short-Term Administration: The most frequent adverse reactions reported during clinical trials were nausea and/or vomiting in 8 of 298 patient treatments (2.7%) and headache in 2 of 298 (0.6%). Less frequent adverse reactions, each of which occurred in 1 of 298 patient treatments (0.3%), included diarrhea, dizziness, anorexia, fatigue, edema, skin rash, leg pain, inguinal adenopathy, medication taste and sore throat.

Long-Term Administration: The most frequent adverse reactions reported in studies of daily therapy for 3 to 6 months were headache in 33 of 251 patients (13.1%), diarrhea in 22 of 251 (8.8%), nausea and/or vomiting in 20 of 251 (8.0%), vertigo in 9 of 251 (3.6%), and arthralgia in 9 of 251 (3.6%). Less frequent adverse reactions, each of which occurred in less than 3% of the 251 patients (see number of patients in parentheses), included skin rash (7), insomnia (4), fatigue (7), fever (4), palpitations (1), sore throat (2), superficial thrombophlebitis (1), muscle cramps (2), pars planitis (1), menstrual abnormality (4), acne (3), lymphadenopathy (2), irritability (1), accelerated hair loss (1), and depression (1).

DOSAGE AND ADMINISTRATION: Treatment of initial genital herpes: One 200 mg capsule every 4 hours, while awake, for a total of 5 capsules daily for 10 days (total 50 capsules).

Chronic suppressive therapy for recurrent disease: One 200 mg capsule 3 times daily for up to 6 months. Some patients may require more drug, up to one 200 mg capsule 5 times daily for up to 6 months.

Intermittent Therapy: One 200 mg capsule every 4 hours, while awake, for a total of 5 capsules daily for 5 days (total 25 capsules). Therapy should be initiated at the earliest sign or symptom (prodrome) of recurrence.

Patients With Acute or Chronic Renal Impairment: One 200 mg capsule every 12 hours is recommended for patients with creatinine clearance ≤ 10 ml/min/1.73/m^2.

HOW SUPPLIED: Zovirax Capsules (blue, opaque) containing 200 mg acyclovir and printed with "Wellcome ZOVIRAX 200"- Bottles of 100 (NDC-0081-0991-55) and unit dose pack of 100 (NDC-0081-0991-56).

Store at 15°-30°C (59°-86°F) and protect from light.

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*In controlled studies, recurrences were totally prevented for 4 to 6 months in up to 75% of patients.

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Bacteremic Hemophilus Influenzae Pneumonia

ROBYN K. GOSHORN, M.D.
Franklin

IT IS INCREASINGLY important that clinicians be aware of Hemophilus influenzae as a respiratory tract pathogen in adults. Improved bacteriologic techniques account for some of the increased frequency of isolation of this organism,[1] but there is evidence of a true increase in the incidence of Hemophilus influenzae pneumonia and bacteremia as well.[2,3] Hemophilus influenzae may be the etiologic agent in 2 to 18% of acute community-acquired pneumonia in adults.[4] These data from the literature support our anecdotal experience at Johnson County Memorial Hospital (a 183-bed community hospital serving a mixed suburban, small town and rural population of approximately 55,000), where we treated three patients with bacteremic Hemophilus influenzae pneumonia in 11 months.

Case Report

A 53-year-old previously healthy housewife became ill suddenly with complaint of sore throat. Pain was of such severity that she had difficulty swallowing and speaking. Outpatient treatment with penicillin resulted in no improvement. Over a 36-hour period her throat pain worsened and she began to complain of dyspnea. Her temperature was 101° Fahrenheit. Indirect laryngoscopic examination revealed inflammation of the pharynx, lingual tonsils, and supraglottic region. Her white blood count was 3,300 with 68 neutrophils (14,13,21,20), 31 lymphocytes, and 1 monocyte.

She was admitted to the hospital and begun on cefoxitin in a dose of 4 grams per 24 hours. On the second hospital day her white blood cell count was 21,000, again with a marked left shift. On the third hospital day she complained of increased dyspnea. A pleural friction rub was heard at the right base, and dullness to percussion and decreased breath sounds were present at both bases. The chest x-ray confirmed bilateral pleural effusions. Arterial blood gases drawn while she was breathing room air showed a PO2 of 58, PCO2 of 32, and a pH of 7.5 A gram stain of pleural fluid revealed small pleomorphic gram-negative rods.

At that time she was begun on cefamandole in a dose of 12 gm. per 24 hours, and bilateral chest tubes were placed. Multiple blood cultures and the pleural fluid cultures subsequently grew Hemophilus influenzae type b biotype II. The organism was resistant to ampicillin but sensitive to chloramphenicol, aminoglycosides, tetracycline, and all cephalosporins tested. She became afebrile. On the 14th day of parenteral antibiotic therapy she developed a recurrence of fever of 102° Fahrenheit. A pericardial friction rub was heard. An echocardiogram showed no pericardial effusion and her chest x-ray was unchanged. Antibiotic therapy was continued in the form of oral tetracycline 2 grams per day, and Ibuprofen 2400 mg. per day was started. Forty ccs. of bloody pleural fluid were obtained by ultrasound guided thoracentesis. Cultures of this fluid were sterile, as were repeat blood cultures.

When all cultures were reported, tetracycline was discontinued. Over the next two months she remained afebrile though she noted dyspnea on exertion such as walking 200 yards. By five months after discharge her exercise tolerance had returned to normal and her chest x-ray was clear, except for minimal pleural thickening at the left base.

Discussion

It has been emphasized in the literature that Hemophilus influenzae pneumonia frequently complicates an underlying disease such as chronic obstructive lung disease, bronchiectasis, and alcoholism.[2,5,6] However, as in the patient presented above, bactermic Hemophilus influenzae pneumonia can occur as a community-acquired infection in a healthy adult with no apparent predisposition. A review of 41 adults with Hemophilus influenzae pneumonia from Houston notes that predisposing conditions were uncommon (20%) in patients under 50.[1]

Several clinical features that can specifically suggest the likelihood of Hemophilus influenzae as the etiologic agent of pneumonia are illustrated by the above case. These features include the abrupt onset of severe upper airway involvement associated with chills and fever,[7] initial leukopenia followed by leukocytosis,[3] and pleural and pericardial involvement.[1,7] Radiographic findings are not specific for Hemophilus influenzae pneumonia.[3] However, certain radiographic features are typical for this pathogen, including multilobar and bilateral infiltrates and pleural effusions.[1,8] Cavitation and bulging fissures are rare.[8]

Because Hemophilus influenzae is commonly present as a commensal organism in the upper airways of nor-

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mal people and in the lower respiratory tracts of persons with chronic obstructive lung disease, cultures of expectorated sputum are not helpful in diagnosing Hemophilus influenzae pneumonia. Transtracheal aspirates are more reliable sources of culture.[9] Dependence on isolation of Hemophilus influenzae from blood or pleural fluid seriously underestimates the incidence of Hemophilus influenzae as the etiology of pneumonia.[9] Gram stains of sputum may be useful but are often misleading.[3,9] Due to a tendency to bipolar staining and variations in coloration, Hemophilus influenzae may be misinterpreted as pneumococci. Masses of Hemophilus influenzae may blend into the background and appear as amorphous proteinacious material.

Treatment

Ampicillin has traditionally been an effective drug against Hemophilus influenzae. It is clear, however, that the incidence of ampicillin resistance is increasing for both typable and nontypable strains of Hemophilus influenzae.[2,10,11,12] The mechanism of resistance in most instances is plasmid mediated beta lactamase production.[2] However, beta lactamase negative organisms resistant to ampicillin also have been reported.[13] Therefore, testing for beta lactamase production is not an adequate way to screen Hemophilus influenzae for ampicillin susceptibility.

There is much variation in the rate of ampicillin resistance in various parts of the country and in different sub-sets of patients. Nevertheless, enough strains are ampicillin resistant to make this drug unacceptable for initial therapy of critically ill patients infected with Hemophilus influenzae.

Cefamandole shows a consistently low minimum inhibitory concentration to both ampicillin-sensitive and ampicillin-resistant strains and is a useful drug for treating serious infections with Hemophilus influenzae when meningitis is not a consideration.[2] Fortunately, meningitis does not appear to be a common complication of bacteremic Hemophilus influenzae pneumonia in adults.[1,3] There are, however, reports of clinical failure of cefamandole therapy against Hemophilus influenzae which shows in vitro sensitivity to this drug. Markham *et al.* presented evidence that failure of cefamandole in a case of empyema with beta lactamase positive Hemophilus influenzae was due to the inoculum effect.[14]

An increase in incidence of resistance to chloramphenicol among Hemophilus influenzae has been reported.[12] Most strains are susceptible to chloramphenicol, and it continues to be a reliable drug for initial therapy of patients with immediately life-threatening Hemophilus influenzae infections pending determination of the antibiotic susceptibility pattern.

Hemophilus influenzae is generally sensitive to second and third generation cephalosporins, moxalactam,[15] and the combination of ampicillin with clavulanic acid,[4] although clinical experience in treating Hemophilus influenzae infections is less extensive with these drugs than with the older agents.[16]

Summary

Hemophilus influenzae is an increasingly common cause of community-acquired respiratory disease in adults. Ampicillin resistance is common enough among strains of Hemophilus influenzae to make this drug unsatisfactory for initial therapy of immediately life-threatening infections. Chloramphenicol remains a standard in therapy of serious Hemophilus influenzae infections. Second and third generation cephalosporins, moxalactam, and combination of ampicillin with clavulanic acid are also generally effective agents.

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Craniocerebral Wound Ballistics

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Abstract

Although firearm homicides are common and self inflicted gunshot wounds of the brain are now the most popular successful means of suicide for both sexes and are increasing in frequency,[1,2] little consolidated information is available concerning the wound ballistics of craniocerebral firearms injuries. This review examines the mechanisms of brain injury and sudden death from gunshot wounds, including pertinent ballistic physics and the interaction of the bullet, cranium and brain to illustrate the pathophysiology of an increasingly common lethal injury.

EACH CRANIOCEREBRAL GUNSHOT WOUND represents a unique interplay between bullet mass, velocity, design, and the varied forces exerted on that projectile by different target areas in the skull and brain. The ballistic factors discussed, especially those specific to gunshot wounds of the brain, will be seen to occur in relative degrees in any given instance.

Wound severity is most closely correlated to the amount of energy transferred by the bullet to the target tissue. This is shown in the kinetic energy equation:

$$K_E = \frac{M\ (V_1^2 - V_2^2)}{2}$$

M equals bullet mass, V_1 equals the bullet's entrant or striking velocity and V_2 the exit velocity. Wounding energy increases with increasing bullet mass and, more importantly, by the square of increasing bullet velocity. Modern bullets designed for defensive purposes (i.e., hollow-pointed), are engineered to minimize or eliminate exit velocity and thereby maximize energy transfer and wound severity.

The first and most simple wounding mechanism is the laceration and tearing of tissue, accomplished by any projectile that penetrates the cranial vault. Although self-inflicted contact gunshot wounds of the head tend to completely perforate the cranium (the "through and through" gunshot wound) more often than distant wounds, the bullet is retained within the skull more than 70% of the time.[3] A single, non-fragmented bullet may ricochet internally or "skate" along the inner table of the skull 20-25% of the time, causing up to 3 tangential wound tracks.[3,4]

These multiple wound tracks, while sometimes partially discernible on skull radiographs, are not always obvious or marked by bullet fragments. This makes the skull radiograph series unreliable in determining the path of the bullet and therefore the degree of brain involvement, except in completely perforating wounds (which tend not to ricochet).[3] Simple laceration of cerebral vessels by projectiles or indriven bone fragments may also cause indirect infarction of the brain tissue distal to the vascular lesion.[5]

Bullets that do not penetrate the cranium or even "blank" cartridges fired against the head may also give rise to severe underlying brain injury. Non-penetrating bullets may cause injury through a blunt force mechanism, and/or displace fragments of the skull through the dura and into the brain. Blank cartridges may cause blunt-force type injuries to the brain through blast effect and scalp injury through the blow-back effect of the burning propellant gases (discussed later). Intracranial contusions and hematomas may be seen with or without skull fracture, and indriven bone fragments may not be visible on skull radiograph. All of these patients, regardless of neurologic findings, require referral for computerized tomographic scan and neurosurgical evaluation.

Beyond these simple physical injuries, however, the cranium and brain act on the bullet to modify its behavior as a wounding instrument. First, as a bullet enters the skull it may deform or fragment. Deformation of the bullet causes its presenting surface area to increase and allows the tissues to exert more drag force against the bullet.[6] This increased "braking" effect in the brain substance causes a more rapid loss of velocity and hence, greater energy transfer. As bone is the most dense tissue in the body, a bullet striking the cranium undergoes a rapid deceleration, often with a large degree of deformation or fragmentation, combining to allow a maximal degree of energy transfer.

Fragmentation of the bullet (the ultimate in deformation) and fragmentation of the skull both serve to increase brain injury. The fragmenting bullet creates multiple missile tracks and therefore multiple brain wounds as an initial effect. Secondly, since the mass of each fragment is much less

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than that of the original bullet, their decreased individual inertia allows most or all of these fragments to decelerate and remain within the cranium. This reduces exit velocity (V_2) to zero, maximizing energy deposition and brain wounding.[6,7] This effect is increased with non-jacketed, soft-point, hollow-point and "exploding" bullets. (Exploding bullets contain a small explosive charge in the bullet tip, which usually detonates on impact to increase bullet deformation and fragmentation. The actual explosion liberates only a small amount of energy as heat and is insignificant in the wounding process.[5]) The fragmentation effect also explains the devastating effect of shotgun blasts, where each pellet acts in the tissue as a rapidly decelerating fragment of the shotshell load, allowing maximized energy deposition and massive tissue destruction. Finally, fragments of the cranium are commonly driven into the brain, acting as secondary missiles and increasing wound severity.[5,9,10] As these bone fragments are of lower density than metal and are propelled only by the energy they receive from the passing bullet, they remain closer to the entrance wound than the bullet fragments.[8]

Another ballistic factor historically associated with increased wound severity is the yawing (formerly thought to be "tumbling") of the bullet on its linear flight axis. Due to a minor deflection of the bullet's flight by the burst of gases following from the weapon's muzzle, the tail of the bullet oscillates slightly from the linear bullet path. Like any waveform, the amplitude of yaw changes at the air/tissue interface, becoming highly amplified. The bullet may yaw between 90° and 270° relative to its linear path, thereby increasing its "presenting area" with commitant increase in tissue drag force, rate of energy deposition and tissue destruction.[6,11] This is probably a minor factor in most civilian gunshot wounds of the brain due to the relatively shorter length of common handgun bullets and their lower velocity cartridges. However, yaw effects have been demonstrated in an autopsy series of low-velocity, civilian brain gunshot wounds.[4] Yawing bullets also develop lift, i.e., a wing-like effect along the plane of oscillation. While insignificant in air, this also is amplified in tissue, causing erratic, curving wound tracks as the bullet decelerates.[12]

Contact gunshot wounds (where the end of the firearm barrel, or muzzle, is pressed against the head) are commonly seen in suicides and add another mechanism of brain injury. When the weapon is fired, hot gases from the burning propellant follow the bullet and are injected into the scalp, meninges and brain. These gases expand explosively as they emerge from the muzzle at very high pressures. Stellate "blow-back" lacerations of the scalp entrance wound are created as these gases dissect beneath the skin at high pressure, and blow back toward the muzzle of the weapon. This effect also extends and increases the severity of the brain wound as the gases enter the cranial vault after the bullet, in part by pressurizing and increasing the brain wound cavity.[3,4,11,13] In the case of contact highpowered rifle and shotgun wounds, with their large amount of exploding propellant, this pressure is thought to contribute significantly to the explosive comminuted skull fractures observed and concomitant "pulpefaction of the brain".[6,11]

Possibly the most important ballistic effect contributing to sudden death in gunshot wounds of the brain is the phenomenon of temporary wound cavitation.[2,4,6,7,8,10] When a bullet strikes the brain, tissue is exploded radially away from the bullet path as kinetic missile energy is transmitted to the brain substance, producing immediate contusion and necrosis due to shearing forces.[5]

This forms a temporary cavity along the bullet path, the volume and configuration of which depend on the striking energy of the bullet and the rate at which the missile's energy is deposited.[6,10] For example, variability is seen in wound cavities from deforming and yawing bullets as the rate of their energy deposition changes.[6] Temporary cavitation occurs in almost all bullet wounds to some degree, and cavities up to 30 times the bullet diameter have been demonstrated in high velocity wounds.[6,10] This cavity pulsates during the milliseconds it exists, then collapses to form the smaller permanent wound cavity.[6] As previously noted, the highly pressurized gases present in contact wounds act to increase this effect.

'Many Mechanisms Interplay to Determine the Severity of a Brain Gunshot Wound'

Intracranial pressure is greatly elevated during temporary cavity formation, exceeding 200 ATM in high-velocity wounds.[11] This reflects the pressure of instantaneous wound cavitation and forces transmitted by compressing the brain against the skull. For example, bursting cranial fractures do not occur in an empty experimental skull (model) when struck by high-energy missiles, because no cavitation occurs in the absence of brain or gel substitute and no pressure is transmitted to the cranial vault. However, these explosive fractures are easily demonstrated in skulls filled with brain substitute and are seen in human craniocerebral gunshot victims.[4,8,11]

The violent compression of tissues away from the temporary wound cavity and resultant instantaneously increased intracranial pressure has also been shown to cause injury distant to the bullet entrance and wound track

even in low-velocity civilian brain gunshot wounds.[3,4] Remote frontal (orbital) lobe contusions are seen, again due to temporary cavitation pressures often high enough to concomitantly fracture the orbital roof.[5] Forensic studies have also consistently demonstrated contusions near the mammillary bodies and of the uncal gyri, cerebellar tonsils and adjacent medulla oblongata associated with remote supratentorial wounds. This evidence of both transtentorial and cerebellar (tonsillar) herniation is due to temporary cavitation and the resultant displacement of brain structures against or through their respective foramina. These contusions are found in the absence of any other possible cause, i.e., cerebral edema or expanding mass lesion.[4,13] In the emergency department setting, consistent clinical findings (apnea, bradycardia) are seen in patients with "minimally abnormal" computerized tomographic scans of the head, again displaying no edema, midline shift or expanding mass.[8] These findings support instantaneous cerebellar (tonsillar) herniation and medullary brainstem compression secondary to temporary massive increase in intracranial pressure as the cause of sudden irreversible coma or death in those gunshot wounds of the brain that do not directly involve vital (brainstem) structures.[3,4,8,10,13,14]

As discussed, many mechanisms interplay to determine the severity of a brain gunshot wound. This is further illustrated by several examples in the literature of suicide by multiple self-inflicted gunshot wounds to the brain.[15,16] In these cases the initial wound does not transmit sufficient energy to cause coma or death, allowing a second (or even third) lethal wound to be self-inflicted by the victim. There is obviously no difference in the weapon caliber, bullet design, or craniocerebral target, but their interrelation changes to cause wounds of different magnitudes. It follows that there may be a certain "quantum" of deposited energy necessary to produce a lethal brain wound, a function of those factors previously discussed in the physical interaction between the wounding projectile, cranium, and brain.

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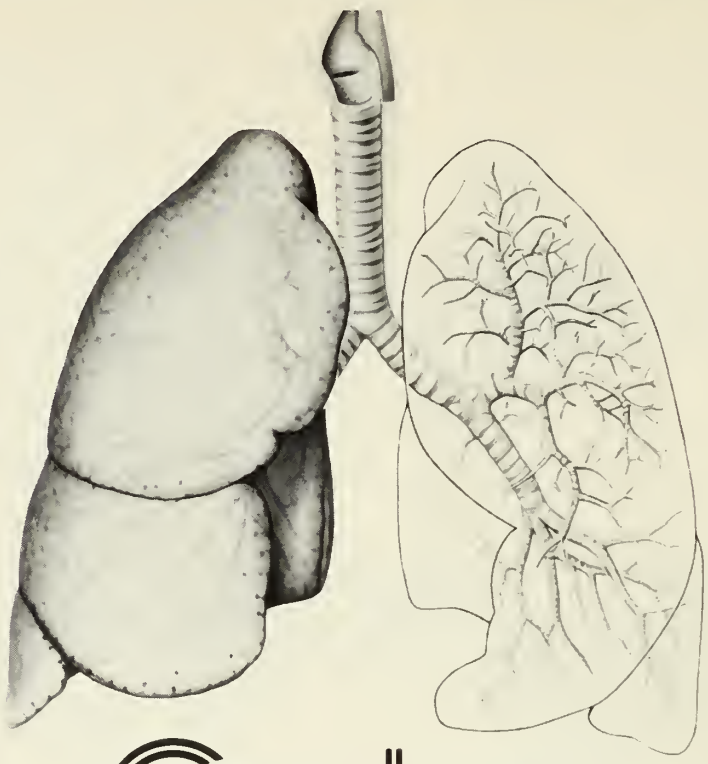
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Anti-Arrhythmic Agents

Update on New Drugs and Their Classification (Part 1)

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DEATHS ATTRIBUTED TO cardiovascular diseases have decreased by approximately 20% in the past two decades. This has been attributed to lifestyle changes emphasizing prudent diet and daily exercise coupled with smoking cessation and weight reduction.[1] Coronary care units, myocardial revascularization surgery and widespread utilization of "new" medicines such as diuretics, beta blockers and calcium channel antagonists in patients with coronary disease and hypertension likely play some role as well.[2]

Despite the statistics showing improved survival, the phenomenon of sudden cardiac death (SCD) remains a significant one for the practitioner. Loss of a patient from left ventricular power failure following large myocardial infarction becomes almost bearable when compared to the frustration of learning one's patient died suddenly while functioning at home, at work, or at play. These patients with adequate functional capacity who die suddenly have aptly been termed "hearts too good to die."

Considerable research has been devoted to SCD over the past decade. It is now possible to identify with some degree of statistical confidence those individuals at increased risk for SCD. The two major warning signs are *left ventricular dysfunction* with or without left ventricular aneurysm formation and *electrical instability* manifesting as complex ventricular arrhythmias recorded on Holter monitoring or provoked by other types of testing such as treadmill stress testing or programmed electrical stimulation studies.[3-5] Very recently, a new focus has been centered on the triggering events for sudden death such as acute ischemia, emotional stress, etc., but clinically applicable conclusions remain forthcoming.[6-9]

Along with our growing understanding of the phenomena of SCD, comes renewed interest in anti-arrhythmic medications for primary prevention. Several new pharmacologic agents have recently been released for clinical use including tocainide, flecainide, mexiletine, and amiodarone. It seems appropriate to summarize their effects and side effects at this time as well as their relationship to the more traditional anti-arrhythmics such as quinidine.

A simplified classification of anti-arrhythmic agents useful for treatment of complex ventricular arrhythmias (and, by implication, *possibly* for SCD) is listed in *Table 1*.[10] Note that several agents cross category boundaries. For example, amiodarone has Class I, III and IV activities, while sotalol has Class II and III activity. A brief summary of these agents, clinical utility, side effects, useful combinations, and contraindications follows. (The Class I agents will be covered this month and Classes II, III and IV next month.)

Class I: the Class I anti-arrythmics achieve their primary antiarrhythmic effect by sodium (fast) channel blockade.[11] Until recently, the only available drugs in this class were quinidine, procainamide, and disopyramide. In vivo, these three drugs prolong myocardial refractoriness more than they slow conduction velocity and this is reflected in their effect on the surface electrocardiogram (ECG): Initial low doses result in QT interval prolongation while higher, often toxic, drug levels cause prolongation of the QRS duration. When lidocaine was recognized as having an anti-arrhythmic effect through sodium channel blockade, it became obvious that the classification system required expansion as lidocaine does not prolong the QT interval before toxic levels are achieved. Lidocaine, therefore, is classed as a IB drug along with its oral analogs, tocainide and mexiletine.

Other sodium channel blockers have subsequently been found to slow conduction velocity more than they prolong refractoriness, e.g., flecainide, propafenone. Therefore, these drugs prolong the PR interval and QRS duration

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with only slight, if any, effect on the QT interval and are arbitrarily assigned to Class IC. The IC drugs, as a group, are reported to be very successful in suppressing ventricular premature contractions. They are also quite useful for slowing conduction through an accessory (Bundle of Kent) pathway. Any and all of the Class I A, B and C drugs have been utilized alone and in combination for the treatment of significant ventricular arrhythmias. It is important to recognize that a *pro-arrhythmic effect* (worsening of the arrhythmia) may be observed in a small but significant percentage (up to 20%) of patients started on these drugs.[12] This is particularly likely to occur when a prolonged QT_c interval is present on the electrocardiogram. Also the QRS complex should never be allowed to increase by more than 25% of its original duration. A brief summary of available and soon to be released Class I antiarrhythmics follows (see *Table 2*):

TABLE 1
Anti-Arrhythmic Drug Classification (Based on Electrophysiologic Similarities)

I. Sodium (fast) channel blockers—delay sodium entry prolonging rate of rise/fall of action potential
   - A. Quinidine, procainamide, disopyramide, pirmenol (prolong refractoriness: increased QT, QRS on ECG)
   - B. Lidocaine, tocainide, mexiletine (no significant ECG changes)
   - C. Flecainide, propafenone, encainide, lorcainide, ethmozine, cibenzoline (prolong conduction velocity; increased PR, QRS on ECG)

II. Beta-Blockers—limit adrenergic responsiveness
   - A. Non-selective: propanolol, sotalol, timolol
   - B. B_1-selective: metoprolol, atenolol
   - C. Non-selective with ISA: pindolol, oxprenolol
   - D. B_1-selective with ISA: acebutolol

III. Potassium Channel Blockers—delay potassium efflux prolonging action potential
   - A. Bretylium tosylate, bethanidine sulfate, ("guanethidine-like" agents)
   - B. Amiodarone (also has weak Class IA, II, IV activity and affects thyroid function)
   - C. Sotolol (also has significant Class II activity)
   - D. N-acetyl procainamide (NAPA)

IV. Calcium Channel Blockers—delay calcium entry, slowing automaticity
   - A. Verapamil, diltiazem, gallopamil, tiapamil (*in vivo* myocardial, electrophysiologic and vascular effects)
   - B. Nifedipine, nitrendipine, nisoldipine, nimodipine, nicardipine, niludipine, felodipine (vascular effects predominate *in vivo*)
   - C. Cinnarizine, flunarizine (peripheral vascular effects predominate)
   - D. Bepridil, lidoflazine, perhexiline (block both slow (Ca^{++}) and fast (Na^{+}) channels)

abbr: QT = QT interval, QRS = QRS duration, ECG = electrocardiogram, PR = PR interval, ISA = intrinsic sympathomimetic activity.

Quinidine sulfate

Quinidine sulfate is the prototype anti-arrhythmic drug. It has a long history of clinical efficacy, both for superventricular and ventricular arrhythmias. Minor side effects are common, and include gastrointestinal upset, diarrhea, and a metallic taste. These side effects often may be managed by switching to a long-acting tablet (Quinidex®) or the gluconate analog (Quinaglute®). Aluminium hydroxide containing antacids such as Amphogel® may alleviate quinidine-induced diarrhea. Quinidine levels are available in most hospitals and clinics as an aid to direct dosage levels and frequency. Close attention to the QT interval and serum quinidine level minimizes toxicity as well as the pro-arrhythmic effect. Like other anti-arrhythmic agents, starting administration in the hospital while the patient is monitored for the first several doses minimizes pro-arrhythmic risks.

Quinidine is useful in combination with other IA drugs, such as procainamide and disopyramide, when it is necessary to maximize therapeutic effect while minimizing individual side effects. Also it may be combined with tocainide, mexiletine or amiodarone. Quinidine does have significant effects on the drug levels of other agents, particularly digoxin. It is recommended that the usual dose of digoxin be halved when adding quinidine.

Procainamide

Procainamide is a topical anesthetic agent which has an electrophysiologic effect similar to quinidine. Ready availability of an intravenous form facilitates rapid arrhythmia control, and the switch to an oral form in the dose needed to achieve serum levels similar to those effective IV is straighforward. Procainamide tablets are very seldom used any longer, due to their short half-life. The new sustained release forms (e.g., Procan SR®) are preferred as they produce adequate blood levels on q6 or 8 hr dosing.

The most significant drawback to the chronic administration of procainamide is its side effect profile. A

TABLE 2
Clinical Profile of Class I Anti-arrhythmics

Drug	Metabolism	Adverse Hemodynamic Effects	Side Effects (minor)	Side Effects (severe)	Usual Dose
Quinidine	hepatic	mild	G.I.	fever, hemolysis, hepatitis	sulfate : 200mg q6h gluconate : 324mg q8h
Procainamide	renal	mild	rash, arthralgia	lupus syndrome	SR capsule : 500-1000mg q6h
Disopyramide	hepatic	serious	anticholinergic	acute urinary retention acute glaucoma congestive heart failure	tablet : 150mg q8h CR : 100-200mg q12h
Pirmenol	1/2 hepatic 1/2 renal	mild	anticholinergic		150mg q8h
Tocainide	2/3 hepatic 1/3 renal	mild	CNS, G.I.		400-600mg q8h
Mexiletine	hepatic	mild	CNS, G.I.		200-400mg q6-8h
Flecainide	hepatic	moderate	CNS, G.I.	congestive heart failure AV block	100-200mg q12h
Propafenone	hepatic	moderate	G.I.	aplastic anemia seizures	150-300mg q8h
Encainide	hepatic	mild	CNS, G.I.		25-50mg q6-8h
Lorcainide	hepatic	mild	CNS, G.I.	vivid nightmares	100-200mg q8-12h
Indecainide	renal	mild	CNS, orthostasis	hepatitis, blurred vision	50-100mg q8h
Ethmozine	hepatic	mild	CNS, G.I.	visual disturbance urinary retention	200-400mg q8h
Cibenzoline	2/3 renal 1/3 hepatic	mild	CNS, G.I. anticholinergic	hepatitis	130-260mg q12h

Abbreviations: G.I. = gastrointestinal, CNS = central nervous system

lupus-like syndrome develops in virtually all patients who are maintained on the medication for over one year. Arthralgia, rash, cerebritis, nephritis, hemolysis and serositis may occur. A positive test for anti-nuclear antibody occurs within several months after beginning procainamide in virtually all individuals. For this reason, procainamide is most useful for treatment of acute arrhythmias associated with myocardial revascularization surgery or myocardial infarction where treatment for three to six months is anticipated but long-term therapy over years is seldom required.

Disopyramide

Disopyramide is another drug similar to quinidine in mode of action. It has a very different side effect profile from quinidine or procainamide, and therein lies its clinical utility. It has a more prominent negative inotropic effect than either quinidine or procainamide and consequently should be used with great caution in patients with left ventricular dysfunction. Due to its atropine-like effects, disopyramide often causes difficulty with visual accommodation and urinary retention, particularly in men with prostate hypertrophy. A long-acting formulation of disopyramide (Norpace CR®) permitting b.i.d. dosing has helped compliance considerably.

Pirmenol

Pirmenol hydrocholoride is a pyridine methanol derivative currently undergoing clinical investigation. It has quinidine-like effects, except that it causes little change in atrial refractoriness. It is currently undergoing investigation in both intravenous and oral form. The side effect profile is quite favorable, with the most frequent side effect being a bitter metallic taste observed in 10% of patients. Anti-

cholinergic side effects, such as dry mouth, constipation, and urinary retention also have been noted. It has only a very mild negative inotropic effect. Besides the mild side effect profile, a long (approximately 8 hours) half-life will permit b.i.d. or t.i.d. dosing. When given intravenously, hypotension is unusual with pirmenol, whereas it is not at all uncommon with procainamide, quinidine or disopyramide.[13,14]

Tocainide

Clinicians have suffered considerable frustration in the past when unable to wean a patient from intravenous lidocaine due to recurrent ventricular ectopy. Tocainide, an oral lidocaine analog, was developed to assist in such a situation. Although the crossover efficacy between lidocaine and tocainide is not 100%, their similarities are significant. Tocainide is primarily useful for the treatment of ventricular ectopy and has little or no efficacy in the treatment of supraventricular arrhythmias. The electrophysiologic effects and side effects of tocainide are similar to lidocaine. The most common side effects are related to the central nervous system with confusion, unsteadiness of gait and paresthesias predominating. Gastrointestinal side effects also occur with some frequency. Blood dyscrasias, e.g., aplastic anemia, neutropenia, may occur very rarely. Tocainide causes slight decrease in left ventricular contractility but not nearly so severe as disopyramide. There are few recognized drug interactions with tocainide, and it may be safely combined with digoxin and the beta blockers. Tocainide is often useful in combination with other Class I antiarrhythmics for added efficacy while using lower doses of each to minimize side effects. The usual dose is 400 mg po t.i.d., but often 600 mg t.i.d. is required for therapeutic effect.[15-17]

Mexiletine

Mexiletine is another lidocaine analog just becoming available for use in the United States.[18-21] Like tocainide, mexiletine is well absorbed from the gastrointestinal tract and has a reasonably long half-life following oral administration, permitting t.i.d. dosing. Also, like tocainide and lidocaine, mexiletine does not prolong the QT interval to the extent that the IA antiarrhythmics do. Its adverse effects are mainly confined to the central nervous system and include drowsiness, confusion, dizziness, vertigo, tremor, paresthesias, lightheadedness and poor vision. Gastrointestinal side effects also are observed but may be minimized by dosing at mealtime. The gastric burning that may occur with mexiletine is responsive to antacids.

Mexiletine is a mild negative inotrope. A positive ANA is quite common with mexiletine therapy but lupus-like syndrome is rare clinically. Reports of elevated liver function tests and clinical hepatitis have very rarely been described with both tocainide and mexiletine. The usual dose of mexiletine is 200 mg to 400 mg orally three to four times daily. Since the drug is extensively metabolized in the liver, dosage should be adjusted downward in patients with hepatic dysfunction. Mexiletine is most useful in the treatment of ventricular arrhythmia but, unlike tocainide, it does have some efficacy in atrial arrhythmias such as atrial premature contractions and atrial fibrillation. It is very useful in combination with IA drugs, especially quinidine.

We administered mexiletine to 53 patients with complex ventricular arrhythmias refractory to therapeutic doses of quinidine, procainamide and disopyramide between January 1982 and January 1986. Mexiletine was clinically effective in suppressing the arrhythmias in 15, as measured by continuous telemetry monitoring, Holter monitoring and treadmill exercise testing. Thirteen showed no effect or worsening of their rhythm disturbance with mexiletine and were switched to another investigational agent. Six had good control of the arrhythmias but developed unacceptable side effects requiring discontinuation of mexiletine. (4 G.I., 2 CNS). One patient required the addition of a second antiarrhythmic (quinidine) for adequate arrhythmic control. Eighteen patients died while on mexiletine, 11 suddenly, five with progressive congestive heart failure, and two with progressive cancer (colon, ovarian).

Flecainide

Flecainide markedly slows impulse conduction in all cardiac tissues, especially the His-Purkinje system.[22] It also prolongs refractoriness and reduces membrane excitability. As the former effect predominates, the observed ECG effects are quite different from the Class IA drugs, such as quinidine.[23] Rather than assessing therapeutic effect based on QT prolongation and watching for toxic effects based on QRS prolongation, as one does with the Class IA drugs, flecainide and the other IC drugs cause prolongation of the QRS and PR interval as their initial ECG effect. Flecainide also exerts significant slowing of conduction in assessory pathways (Bundle of Kent) such as seen in Wolff-Parkinson-White syndrome.

Flecainide is extremely useful in the treatment of ventricular premature contractions and has developed a reputation as a "PVC killer." It may be less successful in suppressing ventricular tachycardia or fibrillation. It also has a significant proarrhythmic effect.[24] Flecainide is useful in some supraventricular arrhythmias, particularly those associated with Wolff-Parkinson-White syndrome. Flecainide has a rather potent negative inotropic effect and consequently should be used with caution in patients with left ventricular dysfunction.

Aside from worsening ventricular function, side effects are primarily related to the central nervous system and gastrointestinal tract similar to tocainide and mexiletine. It may be used effectively in combination with the Class IA and IB drugs. Particular caution is recommended when combining

flecainide with disopyramide because the very potent negative inotropic effects of these drugs may be addictive. The usual starting dose of flecainide is 50 mg every 12 hours orally. The effective dose ranges between 100-200 mg bid. The dose should be increased by increments of 100 mg/day only every second or third day due to the prolonged half-life of the drug. More rapid increases in dosage to achieve rapid suppression of the arrhythmia could lead to later toxicity when serum levels increase to steady-state.

Propafenone

Propafenone is an anti-arrhythmic agent presently under investigation in the United States and nearing approval for general use.[25,26] Its pharmacologic and antiarrhythmic effects are very similar to flecainide. Oral absorption is nearly 100% but, interestingly, bioavailability increases as the dosage is increased, suggesting saturable first pass hepatic clearance. Thus, steady state plasma levels increase disproportionately as the dosage is increased. For example, the plasma levels at 900 mg per day are nine times the steady state plasma concentration at 300 mg per day. Therefore, extreme caution must be utilized in increasing the dose of this medication.

Propafenone produces similar changes on the ECG as flecainide and has similar negative inotropic effects. The side effects of propafenone are primarily due to provoking congestive heart failure or advanced AV block. Both flecainide and propafenone should be used with caution in the setting of underlying bundle branch block or AV node disease. Unlike flecainide, neurological side effects, nausea and constipation are rarely reported. Hepatitis, leukopenia, agranulocytosis and seizures have been reported in extremely rare instances. It may be used in combination with other Class IA and IB agents but it should be used with caution in combination with disopyramide because of its negative inotropic effect. Propafenone also is a weak beta and calcium channel blocker. Like quinidine and verapamil, it increases the serum digoxin level.

We have treated 11 patients with propafenone since March 1984, all with refractory VPCs but none with ventricular tachycardia or fibrillation. Five patients had excellent suppression of their VPCs with no side effects. In five, the drug was discontinued: lack of efficacy-2, proarrhythmic effect-2, reversible leukopenia-1. One patient died suddenly while taking propafenone.

Encainide

Encainide is a Class IC agent presently under investigation in the USA. Its electrophysiologic effects are similar to flecainide and propafenone.[27] There are two important metabolites of encainide, O-dimethylencainide (ODE) and 3-methoxy O-dimethylencainide (MODE), which are pharmacologically active and contribute to the anti-arrhythmic facts. ODE is nine times as potent as the parent compound, which has comparable efficacy to MODE.[28] Predominant side effects of encainide include blurring of vision, dizziness, tremor and ataxia. In contrast to flecainide and propafenone, encainide would appear to have only mild negative inotropic effects.

Lorcainide

Lorcainide is another investigational drug with IC electrophysiologic effects.[29] When given orally, it is rapidly metabolized by the liver to norlorcainide, which possesses anti-arrhythmic activity less marked than the parent compound but with a much longer half-life, which stabilizes serum levels. The effects of lorcainide on electrocardiogram are similar to those described for flecainide. Like encainide, lorcainide has only mild negative inotropic effects. The main side effects of lorcainide are related to the central nervous system, with the most common complaint being sleep disorders including insomnia and nightmares. Diaphoresis also has been reported as an unusual side effect with lorcainide.

Indecainide

Indecainide is a IC anti-arrhythmic, structurally similar to aprindine but having fewer side effects. Like the other IC drugs, it significantly prolongs conduction velocity and, to a lesser extent, refractory periods of all cardiac tissues. It has moderate negative inotropic effects.

Ethmozine

Ethmozine is a phenylthiazine derivative developed as an anti-arrhythmic in the Soviet Union in the 1960s. It may be effective for both supraventricular and ventricular arrhythmias.[30] Electrophysiologically, ethmozine significantly depresses the maximum rate of depolarization, especially in hypoxic conditions, while prolonging the effective refractory period and accelerating repolarization. Ethmozine has little effect on left ventricular function. Clinically, ethomozine has little effect in therapeutic doses on EKG parameters, although on rare occasions, widening of the PR and QRS may be observed. The side effects are predominantly CNS including vertigo, dizziness, confusion and paresthesias. Dry mouth, epigastric discomfort, diarrhea and vomiting also have been reported. Visual disturbances may be bothersome. Toxicology studies performed in rats with high doses of ethmozine have shown hepatic carcinoma.

Cibenzoline

Cibenzoline succinate is not chemically related to other known anti-arrhythmic agents and is the first imidazoline derivative recognized to have anti-arrhythmic activity. It prolongs the transmembrane action potential refractory period, decreases the rate of rise of the action potential, prolongs repolarization and blocks the slow inward calcium channel. It therefore possesses features of Class I, III and IV anti-arrhythmic agents.[31] Its clinical efficacy in the suppression of ven-

tricular arrhythmias and treatment of Wolff-Parkinson-White syndrome has been reported in European studies for nearly a decade.

Electrocardiographic changes noted with cibenzoline are similar to flecainide. The main side effects include gastrointestinal discomfort and central nervous complaints. Prominent anticholinergic side effects may be seen similar to disopyramide, with xerostomia and urinary retention. Asymptomatic elevation of liver enzymes may also be noted. The drug has a moderate negative inotropic effect and should be used with caution in individuals with left ventricular dysfunction.

Summary

A simplified classification scheme for clinically useful anti-arrhythmic agents has been outlined and the Class I drugs reviewed. Next month (Part II) attention will focus on Classes II, III and IV.

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Sleep/Wake Laboratory Testing: Indications and Techniques

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IMPROVEMENTS IN CLINICAL sleep/wake laboratory testing (polysomnography) have closely followed rapid advances in basic human sleep physiology and pathophysiology over the past 20 years. The widespread clinical application of these modern sleep/wake diagnostic techniques has resulted in a practical classification of once mysterious afflictions,[1] and the discovery that the sleep/wake disorders are surprisingly common.[2]

For example, each year about 10 million Americans consult a physician about a sleeping problem. Narcolepsy, once thought to be a rare disease, is now known to be the most common cause of chronic pathological somnolence below age 40 with a prevalence of about 4 per 10,000. Some studies suggest that the obstructive sleep apnea syndrome may affect up to 1% of those above age 40. The childhood sleep/wake parasomnias are even more prevalent: Nocturnal enuresis is seen in about 10-15% of otherwise normal 5-year-olds, and persists into adulthood in many.

The increasing lay and professional awareness of sleep/wake disorders has been paralleled by the opening of an increasing number of regulated and unregulated "sleep labs." The Association of Sleep Disorder Centers (ASDC) was formed in 1975 by a multidisciplinary group of sleep specialists from neurology, pulmonary medicine, psychiatry and other specialists to establish, maintain and update standards for sleep centers in the United States and Europe. The ASDC closely regulates member sleep centers to ensure that they possess adequate technical and professional expertise in this complex and rapidly growing field. Unfortunately, there are still many "sleep disorder centers" in the United States that have not been willing or able to meet the ASDC's standards. As a result, technique and quality vary widely in non-ASDC regulated sleep laboratories.

Since the performance and interpretation of sleep/wake testing is complex and time-consuming, it is expensive. Charges for overnight polysomnography range from $700 to over $1,000 nationally. When done correctly, sleep testing can save thousands of dollars in futile waketime testing and guide specific health and life-saving therapy. When done incorrectly, scarce health care resources are wasted and the patient's health jeopardized. The clinician encountering a patient with a possible sleep/wake disorder must be informed about the indications and limitations of this expensive testing and have some means of determining the adequacy of a particular sleep lab, if it is not an accredited member of the ASDC.

The following indications and techniques are derived from position papers of the Association of Sleep Disorder Centers[3,5] and the American College of Chest Physicians.[4] These guidelines constitute the current standards practiced in ASDC sleep/wake centers throughout the USA.

The two sleep tests to be addressed are those most widely performed by sleep/wake centers: the Overnight Polysomnogram and the Multiple Sleep Latency Test.

The Overnight Polysomnogram

The Overnight Polysomnogram objectively measures the duration, depth and quality of a patient's sleep, and detects sleep-related pathology such as sleep apnea, hypoxemia, cardiac arrhythmias and periodic leg movements in sleep. Since obstructive sleep apnea is usually markedly exacerbated by Rapid Eye Movement (REM) sleep, which normally does not occur during the day, it is quite important that the OPSG be done at night. This predilection of REM sleep for night is one of many reasons that "daytime nap studies" to "rule out" sleep apnea are often quite inaccurate and have been abandoned by serious sleep/wake centers.

The detection and quantification of sleep requires the monitoring of electroencephalogram (EEG), extraoculogram (EOG) and submental surface electromyogram (EMG). The detection and quantification of sleep-related cardiopulmonary disorders such as sleep apnea requires the continuous recording of nasal/mouth airflow, thoracic/abdominal respiratory movement and the electrocardiogram. Ear oximetry also should be monitored

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in most patients complaining of excessive waketime somnolence, but not necessarily in those complaining of insomnia unless sleep apnea is suspected. Finally, bilateral anterior tibialis surface EMG should be recorded to screen for sleep myoclonus, a common age related sleep disorder that often clinically mimics sleep apnea.

Because many cardiopulmonary disorders are markedly worsened during sleep, the OPSG should be done in an accredited hospital with a cardiopulmonary resuscitation team readily available throughout the night.

The cardinal sleep/wake symptoms constitute the major indications for the OPSG: excessive waketime somnolence, severe and persistent insomnia (four or more nights per week for three or more months), or unexplained sleep-related abnormal psychomotor behavior. Less common but also important indications for the OPSG include unexplained morning headaches, cor pulmonale, nocturnal cardiac arrhythmias, and erythrocytosis as possible manifestations of occult obstructive sleep apnea. "Excessive" snoring may also be an indication for an OPSG if sleep apnea is strongly suspected. However, it should be realized that while up to 30% of males snore only a small percentage will have obstructive sleep apnea.

The Multiple Sleep Latency Test Electroencephalogram

The Multiple Sleep Latency Test (MSLT)[6] is a modified EEG consisting of four to five daytime nap opportunities spaced at two-hour intervals beginning at 9 or 10 a.m. The patient is asked to try to sleep, and the onset to objective EEG-sleep onset (sleep latency) is precisely measured. Additionally, the presence or absence of abnormal daytime REM-sleep is determined. The measured sleep latencies are then averaged to give the mean sleep latency, which is an objective quantification of daytime somnolence. Since the purpose of the MSLT is to detect and stage sleep, not to detect sleep apnea or myoclonus, only the EEG, EOG and submental EMG need to be monitored.

There are two major indications for the MSLT: 1) the objective measurement of a patient's complaint of waketime somnolence and 2) detection of abnormal daytime REM sleep that is the hallmark of narcolepsy. The MSLT is not indicated for the evaluation of chronic insomnia or abnormal nocturnal psychomotor behavior unless waking hypersomnolence is also suspected.

It is important to verify and quantify the complaint of excessive sleepiness. A sleepy patient's risk of an automobile or other accident is directly proportional to the severity of waking hypersomnolence. It is hazardous to trust the patient's assessment of severity, since hypersomnolent patients usually underestimate their waking impairment (the "dormouse effect"). The MSLT allows confirmation and precise quantification of this target symptom and helps determine the urgency of treatment and need for driving or occupational restrictions.

In the evaluation of the hypersomnolent patient, the greatest diagnostic information is obtained when the MSLT is performed on the day following the OPSG. This allows the degree of measured hypersomnolence to be compared with the quality and quantity of the preceding night's sleep. "Central" causes of waking hypersomnolence such as narcolepsy, primary central nervous system hypersomnolence, etc., result in daytime sleepiness disproportional to the quality of the preceding night's sleep.

Finally, the presence of MSLT-detected daytime REM sleep is virtually diagnostic of narcolepsy if obstructive sleep apnea has been excluded by the preceding night's OPSG.[6]

These sleep tests are among the most demanding in medicine. The performance and scoring of both the OPSG and the MSLT should be done by a well trained technician, preferably a Registered Polysomnographic Technician (R.PSG.T). Interpretation should be performed by a physician well versed in the pitfalls and artifacts of these complex sleep tests, ideally an ASDC Accredited Clinical Polysomnographer (ACP).

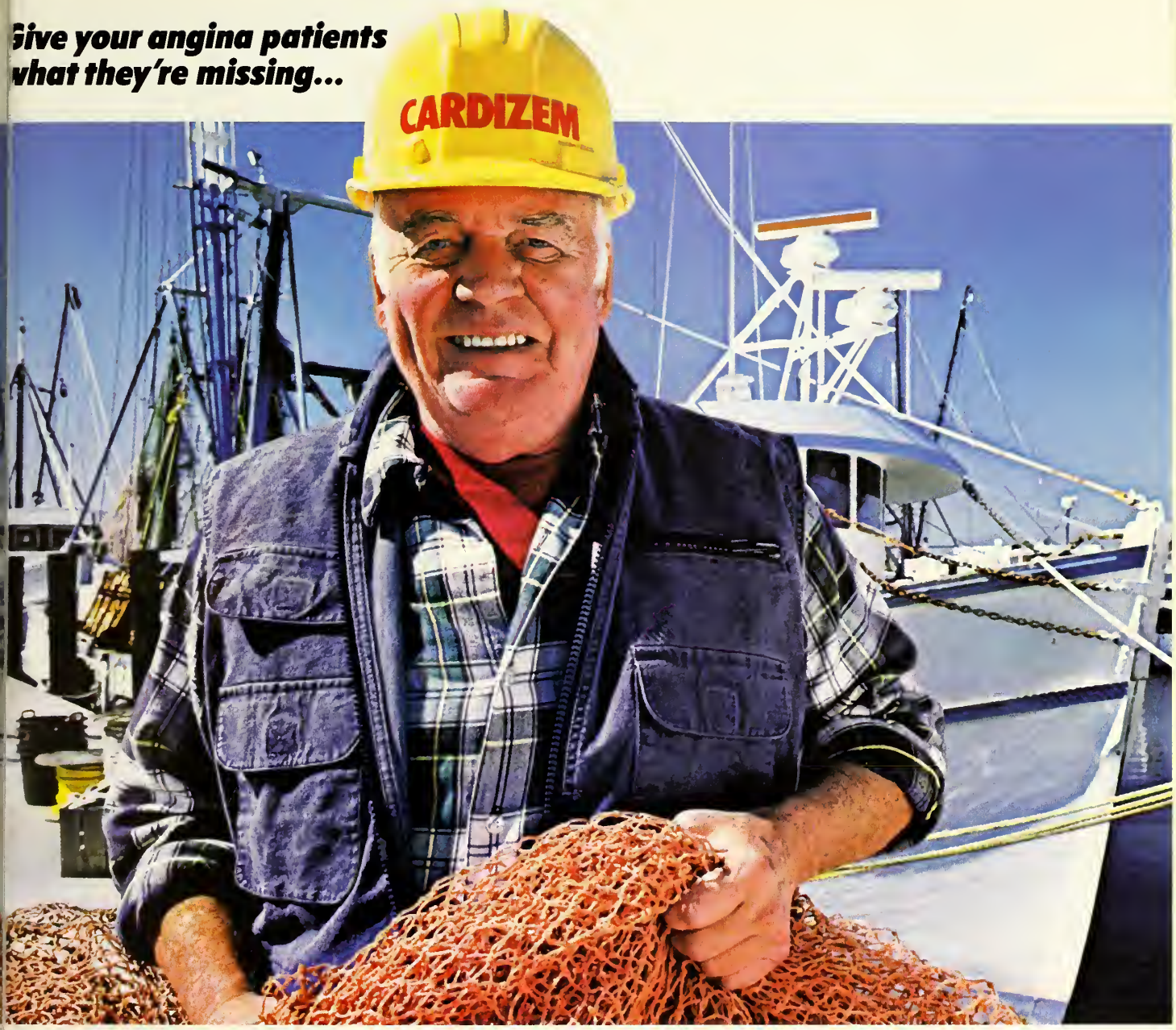
Summary

Sleep/wake disorders are common causes of chronic hypersomnolence, insomnia, and abnormal nocturnal psychomotor behavior. Sleep/wake laboratory testing is usually required for accurate diagnosis and treatment. Unfortunately, many "sleep labs" remain unregulated by the multidisciplinary Association of Sleep Disorders Centers (ASDC) or any other organization. As a result, technique and quality of sleep testing vary widely in non-ASDC accredited centers. Since these tests are expensive, the clinician needs to be informed about their indications, and have some means of determining the adequacy of a particular non-ASDC sleep lab. Standardized indications and techniques for the overnight polysomnogram and multiple sleep latency test have been determined by the ASDC and American College of Chest Physicians and are summarized in this article.

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CONTRAINDICATIONS
CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, and (3) patients with hypotension (less than 90 mm Hg systolic).

WARNINGS

1. ***Cardiac Conduction.*** *CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (six of 1,243 patients for 0.48%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of diltiazem.*
2. ***Congestive Heart Failure.*** *Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt).*
   Experience with the use of CARDIZEM alone or in combination with beta-blockers in patients with impaired ventricular function is very limited. Caution should be exercised when using the drug in such patients.
3. ***Hypotension.*** *Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.*
4. ***Acute Hepatic Injury.*** *In rare instances, significant elevations in enzymes such as alkaline phosphatase, CPK, LDH, SGOT, SGPT, and other symptoms consistent with acute hepatic injury have been noted. These reactions have been reversible upon discontinuation of drug therapy. The relationship to CARDIZEM is uncertain in most cases, but probable in some. (See PRECAUTIONS.)*

PRECAUTIONS
General. *CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any new drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes, however, these changes were reversible with continued dosing.*

Drug Interaction. *Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS.)*

Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers or digitalis is usually well tolerated. Available data are not sufficient, however, to predict the effects of concomitant treatment, particularly in patients with left ventricular dysfunction or cardiac conduction abnormalities. In healthy volunteers, diltiazem has been shown to increase serum digoxin levels up to 20%.

Carcinogenesis, Mutagenesis, Impairment of Fertility. *A 24-month study in rats and a 21-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response in in vitro bacterial tests. No intrinsic effect on fertility was observed in rats.*

Pregnancy. *Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration at doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/postnatal studies, there was some reduction in early individual pup weights and survival rates. There was an increased incidence of stillbirths at doses of 20 times the human dose or greater.*

There are no well-controlled studies in pregnant women, therefore, use CARDIZEM in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. *Diltiazem is excreted in human milk. One report suggests that concentrations in breast milk may approximate serum levels. If use of CARDIZEM is deemed essential, an alternative method of infant feeding should be instituted.*

Pediatric Use. *Safety and effectiveness in children have not been established.*

ADVERSE REACTIONS
Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded.

In domestic placebo-controlled trials, the incidence of adverse reactions reported during CARDIZEM therapy was not greater than that reported during placebo therapy.

The following represent occurrences observed in clinical studies which can be at least reasonably associated with the pharmacology of calcium influx inhibition. In many cases, the relationship to CARDIZEM has not been established. The most common occurrences as well as their frequency of presentation are: edema (2.4%), headache (2.1%), nausea (1.9%), dizziness (1.5%), rash (1.3%), asthenia (1.2%). In addition, the following events were reported infrequently (less than 1%):

Cardiovascular:	*Angina, arrhythmia, AV block (first degree), AV block (second or third degree — see conduction warning), bradycardia, congestive heart failure, flushing, hypotension, palpitations, syncope*
Nervous System:	*Amnesia, gait abnormality, hallucinations, insomnia, nervousness, paresthesia, personality change, somnolence, tinnitus, tremor*
Gastrointestinal:	*Anorexia, constipation, diarrhea, dysgeusia, dyspepsia, mild elevations of alkaline phosphatase, SGOT, SGPT, and LDH (see hepatic warnings), vomiting, weight increase*
Dermatologic:	*Petechiae, pruritus, photosensitivity, urticaria*
Other:	*Amblyopia, dyspnea, epistaxis, eye irritation, hyperglycemia, nasal congestion, nocturia, osteoarticular pain, polyuria, sexual difficulties*

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: alopecia, gingival hyperplasia, erythema multiforme, and leukopenia. However, a definitive cause and effect between these events and CARDIZEM therapy is yet to be established.

Issued 7/8

See complete Professional Use Information before prescribing.

References: ***1.*** *Pepine CJ, Feldman RL, Hill JA, et al: Clinical outcome after treatment of rest angina with calcium blockers: Comparative experience during the initial year of therapy with diltiazem, nifedipine, and verapamil. Am Heart J 1983; 106(6): 1341-1347.* ***2.*** *Shapiro W: Calcium channel blockers: Actions on the heart and uses in ischemic heart disease. Consultant 1984; 24(Dec): 150-159.* ***3.*** *Johnston DL, Lesoway R, Humen DP, et al: Clinical and hemodynamic evaluation of propranolol in combination with verapamil, nifedipine and diltiazem in exertional angina pectoris: A placebo-controlled, double-blind, randomized, crossover study. Am J Cardiol 1985; 55: 680-687.* ***4.*** *Cohn PF, Braunwald E: Chronic ischemic heart disease, in Braunwald E (ed): Heart Disease: A Textbook of Cardiovascular Medicine, ed 2. Philadelphia, WB Saunders Co, 1984, chap. 39.* ***5.*** *Schroeder JS: Calcium and beta blockers in ischemic heart disease: When to use which. Mod Med 1982; 50(Sept): 94-116.*

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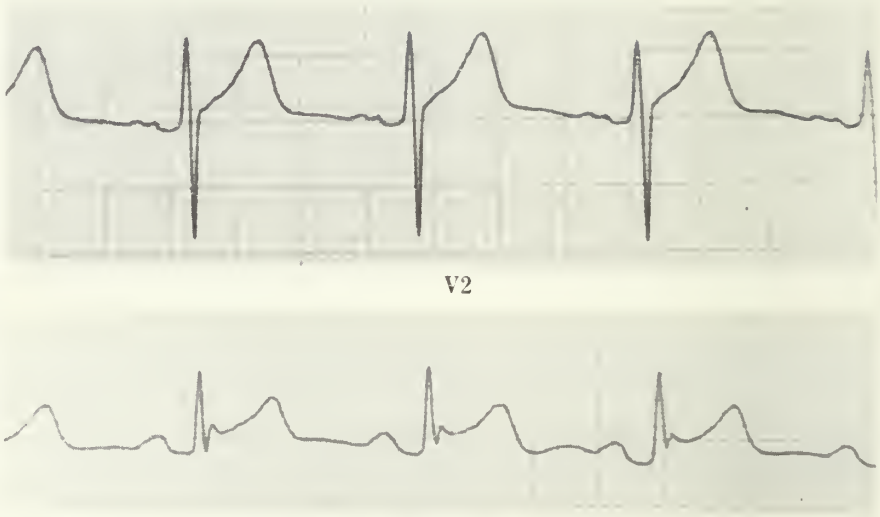
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ATRIAL INFARCTION

MICHAEL E. PAUSZEK, M.D.
Franklin



V2

Lead 2

ATRIAL INFARCTION commonly (17%) complicates ventricular infarction, yet is rarely recognized.[1] The EKG changes are subtle and easily overlooked, and the clinical manifestations are usually attributed to the associated ventricular infarction. However, atrial infarction can cause atrial dysrhythmia, embolization, and occasional atrial rupture.

The SA-node artery and an occasional accessory atrial artery, generally arising from the proximal right coronary artery, provide the vascular supply to the atrium. Even more unusual are reported cases of isolated atrial infarction. Factors contributing to this rarity include the proximal origin of the blood supply, the lack of general recognition of the EKG changes, and the minimal amount of musculature involved, with resultant minimal elevation of CPK.

In a two-year period (1984-1985) of monitoring all infarction patients admitted to the Johnson County Memorial Hospital (total of 160 patients), one case of isolated atrial infarction and a second probable case were identified (incidence of 1.25%). The one case is briefly discussed.

Case Report

A 58-year-old man was admitted on August 31, 1984 for evaluation of chest pain which radiated to the left arm. Initial examination revealed a pale, acutely ill, middle-aged man. The remaining exam was unremarkable. PR (PTa) segment elevation was present in AVL and PR (PTa) segment depression was noted in the inferior leads with notching of the P-waves (see rhythm strip). His CPK peaked at 235 units (normal to 232) with a CKMB of 8 units. Echocardiographic evaluation revealed an enlarged, akinetic right atrium. No ventricular wall motion abnormalities were seen. Initial hospital course was complicated by paroxysmal atrial tachycardia with 2:1 block. The remainder of the hospitalization was uneventful.

Discussion

Atrial infarction is associated with a clinical syndrome identical to ventricular infarction, with pain and diaphoresis as common presenting complaints. It has been largely a post mortem diagnosis. In autopsy series, approximately 20% of atrial infarctions are unassociated with ventricular infarction, with isolated atrial infarction then accounting for 4 to 5% of all myocardial infarctions.[2]

The EKG criteria for the diagnosis of atrial infarction have been verified by both animal model and human autopsy series.[3] The major criteria are: (1) PTa-segment elevation of .5 mm. in V5-V6, with PTa-segment depression of .5 mm. in V1 and V2, or (2) PTa-segment elevation of greater than or equal to .5 mm. in lead 1 and PTa-segment depression of greater than or equal to .5 mm. in lead 2 and lead 3, or (3) PTa-segment depression of greater than or equal to 1.5 mm. in the precordial leads, and 1.2 mm. in leads 1, 2, or 3, with any atrial dysrhythmia. Minor criteria include (1) notched P-waves, (2) depression of any PTa-segment (small amplitude), without elevation of any PTa-segment.

Differentiation of predominant right versus left atrial involvement is suggested by the location of the PTa change, with elevation in leads 1, V5 and V6 consistent with primarily left atrial involvement.

The treatment of atrial infarction is similar to that of ventricular infarction. If the right atrium is predominantly in-

Correspondence: Johnson County Internal Medicine Associates, 1101 W. Jefferson St., Franklin, Ind. 46131.

volved, hypotension should be responsive to volume-loading similar to right ventricular infarction. The mortality rate associated with isolated atrial infarction is unknown.

Summary

A case of isolated atrial infarction is presented. Characteristics included a typical history of chest discomfort, PR (PTa) segment electrocardiographic changes, low total CPK, atrial dysrhythmia and abnormal echocardiographic findings.

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The Effects of Antihypertensive Therapy on the Quality of Life

An Abstract from the New England Journal of Medicine

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GORDON H. WILLIAMS, M.D.

We conducted a multicenter randomized double-blind clinical trial among 626 men with mild to moderate hypertension to determine the effects of captopril, methyldopa, and propranolol on their quality of life. Hydrochlorothiazide was added if needed to control blood pressure.

After a 24-week treatment period, all three groups had similar blood-pressure control, although fewer patients taking propranolol required hydrochlorothiazide. Patients taking captopril alone or in combination with a diuretic were least likely to withdraw from treatment because of adverse effects (8% vs. 20% for methyldopa and 13% for propranolol).

The treatment groups were similar in scores for sleep dysfunction, visual memory, and social participation. However, patients taking captopril, as compared with patients taking methyldopa, scored significantly higher ($P < 0.05$ to < 0.01) on measures of general well-being, had fewer side effects, and had better scores for work performance, visual-motor functioning, and measures of life satisfaction. Patients taking propranolol also reported better work performance than patients taking methyldopa. Patients taking captopril reported fewer side effects and less sexual dysfunction than those taking propranolol and had greater improvement ($P < 0.05$ to < 0.01) on measures of general well-being.

Our findings show that antihypertensive agents have different effects on the quality of life and that these can be meaningfully assessed with available psychosocial measures.

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Medicine's Lighter Moments

TED L. GRISELL, M.D.
Indianapolis

THE CALENDAR

SOMETIMES IT IS A little difficult to understand the reaction certain patients have under stressful conditions that are brought about by the diagnosis of their illnesses.

One night, I was asked to see a patient in the emergency room at one of our local private hospitals. An examination on this particular occasion was somewhat more exciting than usual in view of the fact that the female body I was examining was one of these magnificently attuned physical specimens with all of the parts not only in their proper location but in an unusually gorgeous proportion.

When we concluded our examination, we advised the patient that, unfortunately, all of the tests and so on suggested that she had acute appendicitis. Upon receiving this information, she burst into tears and for a few minutes was almost hysterical. It took some skill on my part to try to assuage her excitement thinking she was fearful of the prospect of surgery, anesthesia and the concomitant illness and recovery period, particularly since she was not native to the city of Indianapolis. She was from Chicago and visiting in Indianapolis.



I advised her that she would probably feel more comfortable if she was with her own physician in Chicago, but I tried to assure her that the expertise of the people who were going to render this emergency surgical care was beyond question, that the hospital services were excellent, the anesthesiologist on call was superior and that, hopefully, my services were in the same category.

Then I discovered that the fear was not for the prospective operation but the fear and trembling was because she thought she would lose her rather highly remunerative job if she had surgery. It turned out that she was one of these individuals whose pictures you will see gracing the walls of automotive repair shops, barber shops and so on, well-known as rather exotic calendar art. She was the body superb that was seen on many of these pin-up type calendars.

When we finally reassured her that the technique we used created no stitch marks and any residual mark could be easily covered with makeup, she was somewhat mollified and finally signed her consent and accepted the operation.

In the bottom of one of my desk drawers, under the cover of a drawer liner, is a group of four or five postoperative photographs that were sent back from Chicago to my office three or four months later which very definitely indicated that there was no mark left by the appendectomy performed that night.

Unfortunately, in the publishing of this opus, it was felt inappropriate to include a copy of this photograph, but if you will go to your local automobile mechanic, barber shop or similar facility, if you look hard enough, I am sure you will find her picture.

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What Every Physician Should Know About Controlled Substance Registration

RONALD L. DYER, J.D.
Indianapolis

EVERY PHYSICIAN who administers, prescribes, or dispenses any controlled substances in Indiana must be registered by the Drug Enforcement Administration and the Indiana Pharmacy Board.

Registration

Indiana physicians are required to register with the Drug Enforcement Administration by applying on Form DEA-224, which can be obtained from the DEA Indianapolis office by calling 317-269-7977. At present, the registration must be renewed annually and the certificate of registration must be maintained at the registered location and kept available for official inspection. This will soon change to a three-year renewal schedule. The annual cost of the DEA registration is currently $20. Every physician now registered with the DEA should receive a re-registration application approximately 45 days before the registration is due to expire. Should one not be received two weeks before the expiration date, call the DEA Indianapolis office.

Beginning June 30, 1987, all Indiana controlled substance registrations will be renewed on June 30 of odd years and notice will be sent along with the Medical Licensing Board registration notice.

The author is Associate Director and General Counsel, Indiana State Medical Association, Indianapolis.

If a physician has more than one office in which controlled substances are administered or dispensed, registration is required at each office. However, if a physician only administers and/or dispenses at a principal office and only writes prescription orders at a second office, registration then is required only at the principal office, provided other offices are within the same state.

All physicians should be registered in drug Schedules II, IIN, III, IIIN, IV, and V, and should therefore check these blocks on both DEA and State applications and re-registration applications.

A physician who moves his or her place of practice, must request modification of the DEA registration by letter to the DEA Indianapolis office, Room 290, 575 N. Pennsylvania St., Indianapolis, Ind. 46204. You must include your old and new addresses, and your DEA registration number. Failure to report a change of address may lead to the seizure of all controlled substances in the physician's possession, as well as administrative or judicial action. Your change of address must also be reported to the Indiana Board of Pharmacy, Health Professions Bureau, Suite 1020, One American Square, Box 82067, Indianapolis, Ind. 46282.

Recordkeeping Requirements

It is necessary for manufacturers, wholesalers, pharmacies, hospitals, and certain physicians, among others, to keep records of drugs purchased, distributed and dispensed.

All controlled substance records must be filed in a readily retrievable manner from all other business documents, retained for two years, and made available for inspection by DEA. "Readily retrievable" means that records are kept so that the controlled drugs listed are asterisked, redlined, or in some other manner visually identifiable apart from other items appearing on the records.

Controlled substance records maintained as part of the patient file must be made available for inspection by DEA. If such records are maintained in patient files, DEA makes a very strict interpretation in requiring those records to be readily retrievable.

Prescribing

A physician who prescribes Schedules II, III, IV, and V controlled substances in the lawful course of professional practice is not required by Federal law to keep records of those prescriptions. However, good medical practice dictates physicians keep some record for their own future reference.

Dispensing

A physician who dispenses controlled substances, including samples, is required to keep a record of each transaction.

Administering

A physician who regularly engages in administering controlled substances in Schedules II, III, IV, and V is required to keep records if patients are charged for these drugs, either separately or together with other professional services. When a physician dispenses a controlled substance and administers this substance, occasionally or regularly from the same inventory, a record of all transactions must be kept.

A physician who occasionally administers a controlled substance, and

does not dispense the controlled substance from the same inventory, is not required by DEA to keep records of these transactions. Again, good medical practice dictates that physicians make some records for their own future reference.

Narcotic Treatment

Records are required for controlled substances dispensed or administered for maintenance or detoxification treatment. A physician is required to be registered separately as a narcotic treatment program to conduct these activities. No controlled substances may be prescribed for maintenance or detoxification under any circumstances.

A physician who dispenses or regularly engages in administering controlled substances, and is required to keep records as stated above, must take an inventory every two years of all stocks of the substances on hand.

Initial Inventory

A physician who intends to conduct any controlled substance activities for which records are required to be maintained must take an inventory of all stocks of controlled substances on hand on the date he or she first engages in such activities or first becomes registered. In the event no controlled substances are on hand at the initial inventory, a zero inventory must be recorded.

The inventory record must:

(1) List the name, address, and DEA registration number of the registrant.

(2) Indicate the date and the time the inventory is taken, i.e., opening or close of business.

(3) Be signed by the person or persons responsible for taking the inventory.

(4) Be maintained at the location appearing on the registration certificate for at least two years.

Records of Schedule II drugs are to be kept separate from all other controlled substances records.

Biennial Inventory

Every two years following the date of the initial inventory, a new inventory is required. The information required on the biennial inventory is the same as that for the initial inventory.

All inventories and records of controlled substances in Schedule II must be maintained separately from all other records of the physician. All inventories and records of controlled substances in Schedules III, IV, and V must be maintained separately or must be in such form that they are readily retrievable from the ordinary professional and business records of the physician.

A physician who has need for controlled drugs in Schedule II for use in the office or medical bag must obtain these drugs by using a triplicate DEA Order Form, not by writing prescriptions made out to "office use." Once received, the Order Form Copy 3 must be noted to show the actual quantity received as well as date of receipt.

Schedules III, IV, and V records: Physicians receiving controlled substances in these Schedules must maintain records of transactions by filling "suppliers," invoices, or maintaining a logbook. Prescriptions may not be written in order to gain these drugs for office use.

Execution of Prescription Orders by Physicians

All prescription orders for controlled substances are to be dated, as of, and signed on, the date when issued and must bear the full name and address of the patient, and the printed name, address, and registration number of the physician. Where an oral order is not permitted, prescription orders must be written in ink, or indelible pencil, or typewritten, and must be manually signed by the practitioner with a signature such as that used by the physician to sign checks. Prescription orders may be prepared by a nurse or secretary for the signature of a physician, but the prescribing physician is responsible in case the prescription order does not conform in all essential respects to the law and regulations.

A written prescription order is required for substances in Schedule II and must be signed by the physician. No one else may sign the prescription on behalf of the physician. The refilling of Schedule II prescription orders is prohibited.

A prescription order for substances in Schedules III and IV may be issued either orally or in writing to the pharm-

Starting June 30, All Indiana Controlled Substance Registrations Will Be Renewed on June 30 of Odd Years

How to Register

Physicians who administer, prescribe or dispense any controlled substances in Indiana must register with the Drug Enforcement Administration and the Indiana Board of Pharmacy. Following are the addresses and telephone numbers:

Drug Enforcement Administration
Indianapolis Office
Room 290
575 N. Pennsylvania St.
Indianapolis, Ind. 46204
(317) 269-7977

Indiana Board of Pharmacy
Health Professions Bureau
Suite 1020
One American Square
Box 82067
Indianapolis, Ind. 46282
(317) 232-2960

acist and may be refilled if so authorized on the prescription. However, the prescription order may only be refilled up to five times within six months after the date of issue. After five refills or after six months, a new prescribing order is required either orally or in writing from the physician. All written prescriptions issued by the physician must bear the signature of the physician. A rubber stamp of the signature or an employee (i.e., nurse) signing the physician's name is not acceptable.

Emergency Telephone Prescription Order for Schedule II Controlled Substances

In the case of a bonafide emergency, a physician may telephone a prescription order to a pharmacist for a controlled substance in Schedule II. In such a case the drug prescribed must be limited to the amount needed to treat the patient only during the emergency period, in no case to exceed a 72-hour supply of the substance. The physician must furnish, within 72 hours, a written, signed prescription order to the pharmacy for the controlled substances prescribed. Should this not be done, the pharmacy is obligated to report the failure to DEA. DEA may then prohibit a physician from issuing further emergency oral prescriptions for Schedule II drugs.

Discontinuance of Practice by a Physician

An Indiana physician who discontinues practice must return his DEA registration certificate and any unused Order Forms to the DEA Indianapolis office. He must also return his Indiana Controlled Substance Registration to the Indiana Pharmacy Board.

Security

A physician who has controlled substances stored in his or her office or clinic must keep the drugs in a securely locked, substantially constructed cabinet or safe.

Thefts or Losses

Any loss or theft of any controlled substance must be reported to the DEA Indianapolis office on a DEA Form 106. You may call them to have the forms sent to you.

Look-Alike and Sound-Alike Drug Names

BENJAMIN TEPLITSKY, R. PH.
Brooklyn, N.Y.

Look-alike and sound-alike drug names can be misinterpreted by a nurse reading doctors' orders or by a pharmacist compounding physicians' prescriptions. Such misunderstandings can result in the administration of a drug not intended by the prescriber. Awareness of such look-alike and sound-alike drug names can reduce potential errors.

	CYCLOSPORINE	CYCLOSERINE
Category:	Immunosuppressive	Antituberculous agent
Brand Name:	Sandimmune, Sandoz	Seromycin, Lilly
Generic Name:	Cyclosporine	Cycloserine
Dosage Forms:	Oral solution, IV solution	Capsules

	CORDRAN	CORDARONE
Category:	Corticosteroid	Antiarrhythmic agent
Brand Name:	Cordran, Dista	Cordarone, Wyeth
Generic Name:	Flurandrenolide	Amiodarone HCl
Dosage Forms:	Ointment, Cream, Lotion, Tape	Tablets

ore prescribing, see complete prescribing information in SK&F CO. rature or *PDR*. The following is a brief summary.

VARNING

his drug is not indicated for initial therapy of edema or hyperten- ion. Edema or hypertension requires therapy titrated to the individual. this combination represents the dosage so determined, its use ay be more convenient in patient management. Treatment of hyper- ension and edema is not static, but must be reevaluated as con- itions in each patient warrant.

traindications: Concomitant use with other potassium-sparing agents h as spironolactone or amiloride. Further use in anuria, progressive al or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum assium. Hypersensitivity to either component or other sulfonamide- ived drugs.

rnings: Do not use potassium supplements, dietary or otherwise, ess hypokalemia develops or dietary intake of potassium is markedly aired. If supplementary potassium is needed, potassium tablets uld not be used. Hyperkalemia can occur, and has been associated n cardiac irregularities. It is more likely in the severely ill, with urine ume less than one liter/day, the elderly and diabetics with suspected onfirmed renal insufficiency. Periodically, serum K^+ levels should be ermined. If hyperkalemia develops, substitute a thiazide alone, restrict intake. **Associated widened QRS complex or arrhythmia requires mpt additional therapy.** Thiazides cross the placental barrier and ear in cord blood. Use in pregnancy requires weighing anticipated efits against possible hazards, including fetal or neonatal jaundice, mbocytopenia, other adverse reactions seen in adults. Thiazides ear and triamterene may appear in breast milk. If their use is essential, patient should stop nursing. Adequate information on use in children ot available. Sensitivity reactions may occur in patients with or with- a history of allergy or bronchial asthma. Possible exacerbation or ivation of systemic lupus erythematosus has been reported with azide diuretics.

cautions: The bioavailability of the hydrochlorothiazide component of azide' is about 50% of the bioavailability of the single entity. oretically, a patient transferred from the single entities of triamterene f hydrochlorothiazide may show an increase in blood pressure or fluid ention. Similarly, it is also possible that the lesser hydrochlorothiazide availability could lead to increased serum potassium levels. However, ensive clinical experience with 'Dyazide' suggests that these conditions e not been commonly observed in clinical practice. Angiotensin- verting enzyme (ACE) inhibitors can elevate serum potassium; use h caution with 'Dyazide'. Do periodic serum electrolyte determinations rticularly important in patients vomiting excessively or receiving enteral fluids, and during concurrent use with amphotericin B or ticosteroids or corticotropin (ACTH)). Periodic BUN and serum atinine determinations should be made, especially in the elderly, betics or those with suspected or confirmed renal insufficiency. mulative effects of the drug may develop in patients with impaired renal ction. Thiazides should be used with caution in patients with impaired iatic function. They can precipitate coma in patients with severe liver ease. Observe regularly for possible blood dyscrasias, liver damage, er idiosyncratic reactions. Blood dyscrasias have been reported in ients receiving triamterene, and leukopenia, thrombocytopenia, anulocytosis, and aplastic and hemolytic anemia have been reported h thiazides. Thiazides may cause manifestation of latent diabetes litus. The effects of oral anticoagulants may be decreased when d concurrently with hydrochlorothiazide; dosage adjustments may be essary. Clinically insignificant reductions in arterial responsiveness orepinephrine have been reported. Thiazides have also been shown to ease the paralyzing effect of nondepolarizing muscle relaxants such tubocurarine. Triamterene is a weak folic acid antagonist. Do periodic od studies in cirrhotics with splenomegaly. Antihypertensive effects y be enhanced in post-sympathectomy patients. Use cautiously in gical patients. Triamterene has been found in renal stones in associa- with the other usual calculus components. Therefore, 'Dyazide' uld be used with caution in patients with histories of stone formation. ew occurrences of acute renal failure have been reported in patients 'Dyazide' when treated with indomethacin. Therefore, caution is ised in administering nonsteroidal anti-inflammatory agents with azide'. The following may occur: transient elevated BUN or creatinine oth, hyperglycemia and glycosuria (diabetic insulin requirements may altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), reasing alkali reserve with possible metabolic acidosis. 'Dyazide' rferes with fluorescent measurement of quinidine. Hypokalemia is ommon with 'Dyazide', but should it develop, corrective measures uld be taken such as potassium supplementation or increased dietary ke of potassium-rich foods. Corrective measures should be instituted tiously and serum potassium levels determined. Discontinue correc- measures and 'Dyazide' should laboratory values reveal elevated um potassium. Chloride deficit may occur as well as dilutional onatremia. Concurrent use with chlorpropamide may increase the risk evere hyponatremia. Serum PBI levels may decrease without signs hyroid disturbance. Calcium excretion is decreased by thiazides. azide' should be withdrawn before conducting tests for parathyroid ction. Thiazides may add to or potentiate the action of other anti- ertensive drugs. Diuretics reduce renal clearance of lithium and ease the risk of lithium toxicity.

erse Reactions: Muscle cramps, weakness, dizziness, headache, mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other matological conditions; nausea and vomiting, diarrhea, constipation, er gastrointestinal disturbances; postural hypotension (may be ravated by alcohol, barbiturates, or narcotics). Necrotizing vasculitis, esthesias, icterus, pancreatitis, xanthopsia and respiratory distress uding pneumonitis and pulmonary edema, transient blurred vision, adenitis, and vertigo have occurred with thiazides alone. Triamterene been found in renal stones in association with other usual calculus ponents. Rare incidents of acute interstitial nephritis have been orted. Impotence has been reported in a few patients on 'Dyazide', ough a causal relationship has not been established.

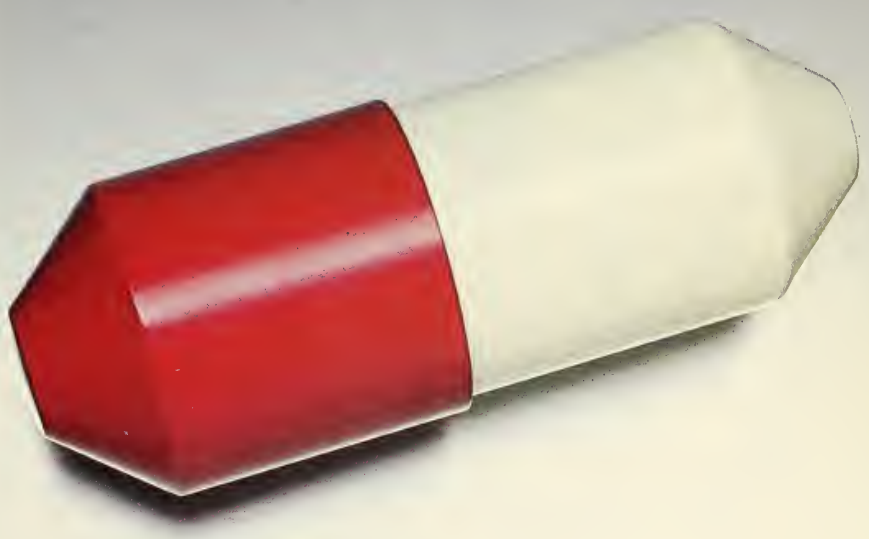
plied: 'Dyazide' is supplied as a red and white capsule, in bottles of 0 capsules; Single Unit Packages (unit-dose) of 100 (intended for itutional use only); in Patient-Pak™ unit-of-use bottles of 100.

S-DZ:L42

In Hypertension*... When You Need to Conserve K^+

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Serum K^+ and BUN should be checked periodically (see Warnings and Precautions).



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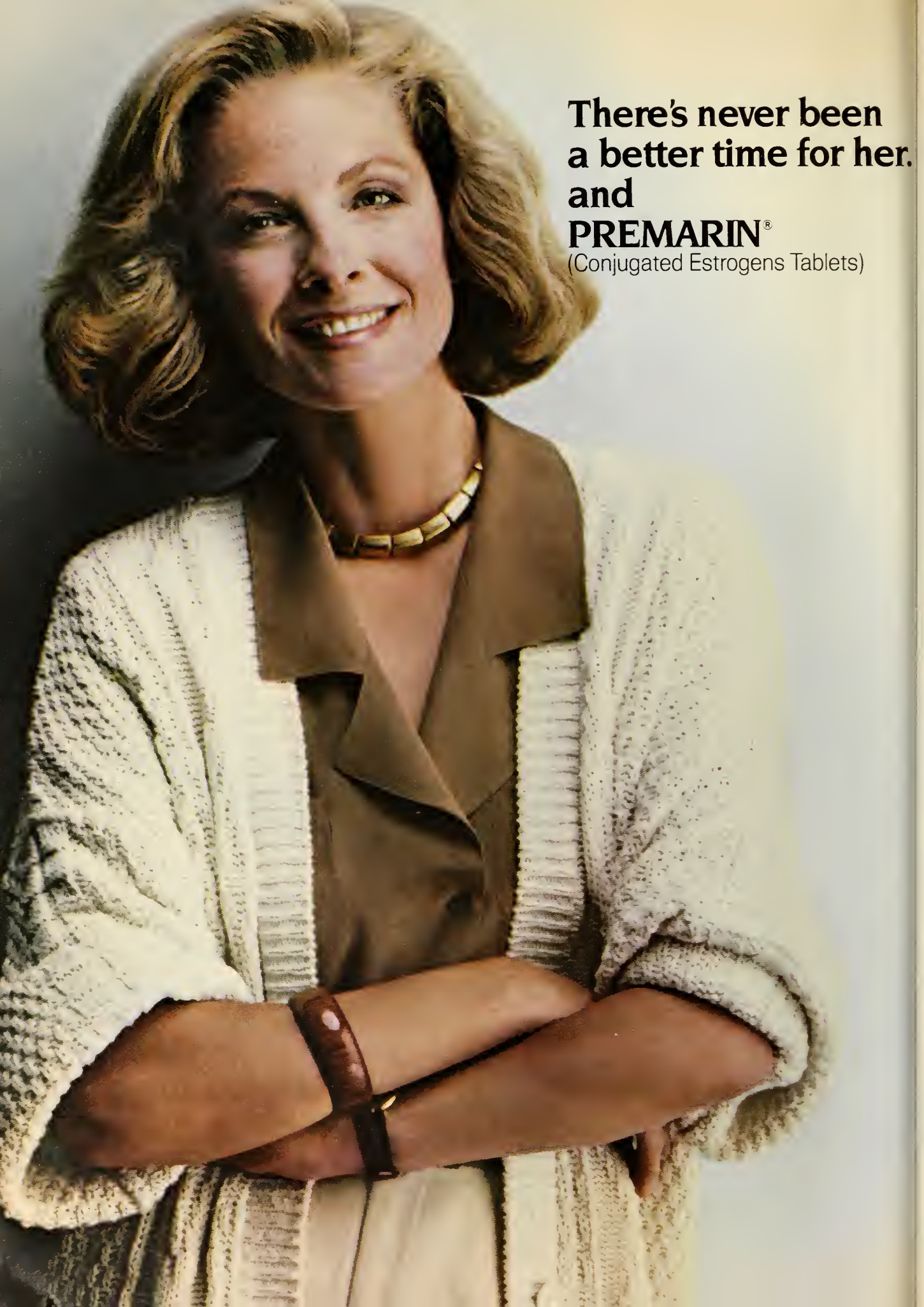
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There's never been a better time for her. and PREMARIN®
(Conjugated Estrogens Tablets)

Now the evidence looks better than ever

Significantly reduced risk of endometrial hyperplasia

Endometrial hyperplasia was significantly reduced when progestin was added to PREMARIN therapy for more than ten days a month.[1-4] The risk of endometrial hyperplasia may also be reduced through cyclic administration of unopposed, low-dose PREMARIN.

Effect on lipids—an important feature

PREMARIN used alone does not adversely affect lipid levels. In fact, a clinical study has shown a significant increase in HDL cholesterol—from 49.7 mg/dL to 56.4 mg/dL—and decrease in LDL cholesterol—from 165.1 mg/dL to 138.1 mg/dL—after one year of therapy with PREMARIN, 0.625 mg.[5]

Low-dose control of menopausal symptoms*

PREMARIN effectively relieves vasomotor symptoms, such as hot flashes. When estrogen deficiency is limited to atrophic vaginitis, PREMARIN® (conjugated estrogens) Vaginal Cream restores the vaginal environment to its premenopausal state.

The most widely used, most extensively studied estrogen worldwide.

PREMARIN®
(Conjugated Estrogens Tablets)

Most trusted for more reasons

*PREMARIN is indicated for moderate-to-severe vasomotor symptoms.

Please see following page for brief summary of prescribing information.

For moderate-to-severe vasomotor symptoms

PREMARIN®
(Conjugated Estrogens Tablets)



0.3 mg 0.625 mg 0.9 mg 1.25 mg 2.5 mg

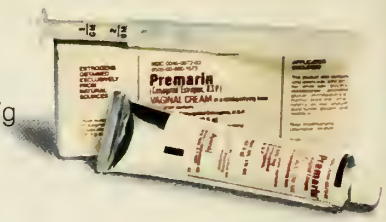
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For atrophic vaginitis

PREMARIN®
(Conjugated Estrogens)

Vaginal Cream

0.625mg/g



BRIEF SUMMARY *(FOR FULL PRESCRIBING INFORMATION AND PATIENT INFORMATION, SEE PACKAGE CIRCULARS.)*

PREMARIN® Brand of conjugated estrogens tablets, USP
PREMARIN® Brand of conjugated estrogens Vaginal Cream in a nonliquefying base

1. ESTROGENS HAVE BEEN REPORTED TO INCREASE THE RISK OF ENDOMETRIAL CARCINOMA.

Three independent case control studies have reported an increased risk of endometrial cancer in postmenopausal women exposed to exogenous estrogens for more than one year. This risk was independent of the other known risk factors for endometrial cancer. These studies are further supported by the finding that incidence rates of endometrial cancer have increased sharply since 1969 in eight different areas of the United States with population-based cancer reporting systems, an increase which may be related to the rapidly expanding use of estrogens during the last decade. The three case control studies reported that the risk of endometrial cancer in estrogen users was about 4.5 to 13.9 times greater than in nonusers. The risk appears to depend on both duration of treatment and on estrogen dose. In view of these findings, when estrogens are used for the treatment of menopausal symptoms, the lowest dose that will control symptoms should be utilized and medication should be discontinued as soon as possible. When prolonged treatment is medically indicated, the patient should be reassessed on at least a semiannual basis to determine the need for continued therapy. Although the evidence must be considered preliminary, one study suggests that cyclic administration of low doses of estrogen may carry less risk than continuous administration; it therefore appears prudent to utilize such a regimen. Close clinical surveillance of all women taking estrogens is important. In all cases of undiagnosed persistent or recurring abnormal vaginal bleeding, adequate diagnostic measures should be undertaken to rule out malignancy. There is no evidence at present that "natural" estrogens are more or less hazardous than "synthetic" estrogens at equiestrogenic doses.

2. ESTROGENS SHOULD NOT BE USED DURING PREGNANCY.

The use of female sex hormones, both estrogens and progestogens, during early pregnancy may seriously damage the offspring. It has been shown that females exposed in utero to diethylstilbestrol, a non-steroidal estrogen, have an increased risk of developing in later life a form of vaginal or cervical cancer that is ordinarily extremely rare. This risk has been estimated as not greater than 4 per 1,000 exposures. Furthermore, a high percentage of such exposed women (from 30% to 90%) have been found to have vaginal adenosis, epithelial changes of the vagina and cervix. Although these changes are histologically benign, it is not known whether they are precursors of malignancy. Although similar data are not available with the use of other estrogens, it cannot be presumed they would not induce similar changes. Several reports suggest an association between intrauterine exposure to female sex hormones and congenital anomalies, including congenital heart defects and limb reduction defects. One case control study estimated a 4.7-fold increased risk of limb reduction defects in infants exposed in utero to sex hormones (oral contraceptives, hormone withdrawal tests for pregnancy, or attempted treatment for threatened abortion). Some of these exposures were very short and involved only a few days of treatment. The data suggest that the risk of limb reduction defects in exposed fetuses is somewhat less than 1 per 1,000. In the past, female sex hormones have been used during pregnancy in an attempt to treat threatened or habitual abortion. There is considerable evidence that estrogens are ineffective for these indications, and there is no evidence from well controlled studies that progestogens are effective for these uses. If PREMARIN is used during pregnancy, or if the patient becomes pregnant while taking this drug, she should be apprised of the potential risks to the fetus, and the advisability of pregnancy continuation.

DESCRIPTION: PREMARIN (conjugated estrogens, USP) contains a mixture of estrogens, obtained exclusively from natural sources, blended to represent the average composition of material derived from pregnant mares' urine. It contains estrone, equilin, and 17α-dihydroequilin, together with smaller amounts of 17α-estradiol, equilenin, and 17α-dihydroequilenin as salts of their sulfate esters. Tablets are available in 0.3 mg, 0.625 mg, 0.9 mg, 1.25 mg, and 2.5 mg strengths of conjugated estrogens. Cream is available as 0.625 mg conjugated estrogens per gram.

INDICATIONS AND USAGE: PREMARIN (conjugated estrogens tablets, USP): Moderate-to-severe *vasomotor* symptoms associated with the menopause. (There is no evidence that estrogens are effective for nervous symptoms or depression without associated vasomotor symptoms and they should not be used to treat such conditions.) **Osteoporosis (abnormally low bone mass).** Atrophic vaginitis. Kraurosis vulvae. Female castration.

PREMARIN (conjugated estrogens) Vaginal Cream is indicated in the treatment of atrophic vaginitis and kraurosis vulvae. PREMARIN HAS NOT BEEN SHOWN TO BE EFFECTIVE FOR ANY PURPOSE DURING PREGNANCY AND ITS USE MAY CAUSE SEVERE HARM TO THE FETUS (SEE BOXED WARNING).

Concomitant Progestin Use: The lowest effective dose appropriate for the specific indication should be utilized. Studies of the addition of a progestin for 7 or more days of a cycle of estrogen administration have reported a lowered incidence of endometrial hyperplasia. Morphological and biochemical studies of the endometrium suggest that 10 to 13 days of progestin are needed to provide maximal maturation of the endometrium and to eliminate any hyperplastic changes. Whether this will provide protection from endometrial carcinoma has not been clearly established. There are possible additional risks which may be associated with the inclusion of progestin in estrogen replacement regimens. (See PRECAUTIONS.) The choice of progestin and dosage may be important; product labeling should be reviewed to minimize possible adverse effects.

CONTRAINDICATIONS: Estrogens should not be used in women (or men) with any of the following conditions: 1. Known or suspected cancer of the breast except in appropriately selected patients being treated for metastatic disease. 2. Known or suspected estrogen-dependent neoplasia. 3. Known or suspected pregnancy. (See Boxed Warning.) 4. Undiagnosed abnormal genital bleeding. 5. Active thrombophlebitis or thromboembolic disorders. 6. A past history of thrombophlebitis, thrombosis, or thromboembolic disorders associated with previous estrogen use (except when used in treatment of breast or prostatic malignancy).

WARNINGS: Long-term continuous administration of natural and synthetic estrogens in certain animal species increases the frequency of carcinomas of the breast, cervix, vagina, and liver. There are now reports that estrogens increase the risk of carcinoma of the endometrium in humans. (See Boxed Warning.) At the present time there is no satisfactory evidence that estrogens given to postmenopausal women increase the risk of cancer of the breast, although a recent study has raised this possibility. There is a need for caution in prescribing estrogens for women with a strong family history of breast cancer or who have breast nodules, fibrocystic disease, or abnormal mammograms. A recent study has reported a 2- to 3-fold increase in the risk of surgically confirmed gallbladder disease in women receiving postmenopausal estrogens.

Adverse effects of oral contraceptives may be expected at the larger doses of estrogen used to treat prostatic or breast cancer or postpartum breast engorgement; it has been shown that there is an increased risk of thrombosis in men receiving estrogens for prostatic cancer and women for postpartum breast engorgement. Users of oral contraceptives have an increased risk of diseases, such as thrombophlebitis, pulmonary embolism, stroke, and myocardial infarction. Cases of retinal thrombosis, mesenteric thrombosis, and optic neuritis have been reported in oral contraceptive users. An increased risk of postsurgery thromboembolic complications has also been reported in users of oral contraceptives. If feasible, estrogen should be discontinued at least 4 weeks before surgery of the type associated with an increased risk of thromboembolism, or during periods of prolonged immobilization. Estrogens should not be used in persons with active thrombophlebitis, thromboembolic disorders, or in persons with a history of such disorders in association with estrogen use. They should be used with caution in patients with cerebral vascular or coronary artery disease. Large doses (5 mg conjugated estrogens per day), comparable to those used to treat cancer of the prostate and breast, have been shown to increase the risk of nonfatal myocardial infarction, pulmonary embolism and thrombophlebitis. When doses of this size are used, any of the thromboembolic and thrombotic adverse effects should be considered a clear risk.

Benign hepatic adenomas should be considered in estrogen users having abdominal pain and tenderness, abdominal mass, or hypovolemic shock. Hepatocellular carcinoma has been reported in women taking estrogen-containing oral contraceptives. Increased blood pressure may occur with use of estrogens in the menopause and blood pressure should be monitored with estrogen use. A worsening of glucose tolerance has been observed in patients on estrogen-containing oral contraceptives. For this reason, diabetic patients should be carefully observed. Estrogens may lead to severe hypercalcemia in patients with breast cancer and bone metastases.

PRECAUTIONS: Physical examination and a complete medical and family history should be taken prior to the initiation of any estrogen therapy with special reference to blood pressure, breasts, abdomen, and pelvic organs, and should include a Papanicolaou smear. As a general rule, estrogen should not be prescribed for longer than one year without another physical examination being performed. Conditions influenced by fluid retention such as asthma, epilepsy, migraine, and cardiac or renal dysfunction, require careful observation. Certain patients may develop manifestations of excessive estrogenic stimulation, such as abnormal or excessive uterine bleeding, mastodynia, etc. Prolonged administration of unopposed estrogen therapy has been reported to increase the risk of endometrial hyperplasia in some patients. Oral contraceptives appear to be associated with an increased incidence of mental depression. Patients with a history of depression should be carefully observed. Preexisting uterine leiomyomata may increase in size during estrogen use. The pathologist should be advised of estrogen therapy when relevant specimens are submitted. If jaundice develops in any patient receiving estrogen, the medication should be discontinued while the cause is investigated. Estrogens should be used with care in patients with impaired liver function, renal insufficiency, metabolic bone diseases associated with hypercalcemia, or in young patients in whom bone growth is not complete. If concomitant progestin therapy is used, potential risks may include adverse effects on carbohydrate and lipid metabolism.

The following changes may be expected with larger doses of estrogen.

a. Increased sulfobromophthalein retention.

b. Increased prothrombin and factors VII, VIII, IX, and X; decreased antithrombin 3; increased norepinephrine-induced platelet aggregability.

c. Increased thyroid binding globulin (TBG) leading to increased circulating total thyroid hormone, as measured by PBI, T4 by column, or T4 by radioimmunoassay. Free T3 resin uptake is decreased, reflecting the elevated TBG; free T4 concentration is unaltered.

d. Impaired glucose tolerance.

e. Decreased pregnanediol excretion.

f. Reduced response to metyrapone test.

g. Reduced serum folate concentration.

h. Increased serum triglyceride and phospholipid concentration. As a general principle, the administration of any drug to nursing mothers should be done only when clearly necessary since many drugs are excreted in human milk.

ADVERSE REACTIONS: The following have been reported with estrogenic therapy, including oral contraceptives: breakthrough bleeding; spotting; change in menstrual flow; dysmenorrhea; premenstrual-like syndrome; amenorrhea during and after treatment; increase in size of uterine fibromyomata; vaginal candidiasis; change in cervical erosion and in degree of cervical secretion; cystitis-like syndrome; tenderness, enlargement, secretion (of breasts); nausea, vomiting; abdominal cramps; bloating; cholestatic jaundice; chloasma or melasma which may persist when drug is discontinued; erythema multiforme; erythema nodosum; hemorrhagic eruption; loss of scalp hair; hirsutism; steepening of corneal curvature; intolerance to contact lenses; headache; migraine; dizziness; mental depression; chorea; increase or decrease in weight; reduced carbohydrate tolerance; aggravation of porphyria; edema; changes in libido.

ACUTE OVERDOSAGE: May cause nausea, and withdrawal bleeding may occur in females.

DOSAGE AND ADMINISTRATION:

PREMARIN® Brand of conjugated estrogens tablets, USP

1. *Given cyclically for short-term use only.* For treatment of moderate to severe *vasomotor* symptoms, atrophic vaginitis, or kraurosis vulvae associated with the menopause (0.3 to 1.25 mg or more daily). The lowest dose that will control symptoms should be chosen and medication should be discontinued as promptly as possible. Administration should be cyclic (eg, three weeks on and one week off). Attempts to discontinue or taper medication should be made at three- to six-month intervals.

2. *Given cyclically:* Female castration. Osteoporosis. Female castration—1.25 mg daily, cyclically. Adjust upward or downward according to response of the patient. For maintenance, adjust dosage to lowest level that will provide effective control. Osteoporosis —0.625 mg daily. Administration should be cyclic (eg, three weeks on and one week off).

Patients with an intact uterus should be monitored for signs of endometrial cancer and appropriate measures taken to rule out malignancy in the event of persistent or recurring abnormal vaginal bleeding.

PREMARIN® Brand of conjugated estrogens Vaginal Cream

Given cyclically for short-term use only. For treatment of atrophic vaginitis or kraurosis vulvae.

The lowest dose that will control symptoms should be chosen and medication should be discontinued as promptly as possible.

Administration should be cyclic (eg, three weeks on and one week off).

Attempts to discontinue or taper medication should be made at three-to-six month intervals.

Usual dosage range: 2 to 4 g daily, intravaginally, depending on the severity of the condition.

Treated patients with an intact uterus should be monitored closely for signs of endometrial cancer and appropriate diagnostic measures should be taken to rule out malignancy in the event of persistent or recurring abnormal vaginal bleeding.

References:

1. Whitehead MI, Townsend PT, Pryse-Davies J, et al: Effects of estrogens and progestins on the biochemistry and morphology of the postmenopausal endometrium. *N Engl J Med* 1981;305:1599-1605. 2. Paterson MEL, Wade-Evans T, Sturdee DW, et al: Endometrial disease after treatment with oestrogens and progestogens in the climacteric. *Br Med J* 1980;280:822-824. 3. Magos AL, Brincat M, Studd JWW, et al: Amenorrhea and endometrial atrophy with continuous oral estrogen and progestogen therapy in postmenopausal women. *Obstet Gynecol* 1985;67:496-499. 4. Whitehead MI, Lane G, Siddle N, et al: Avoidance of endometrial hyperstimulation in estrogen-treated postmenopausal women. *Semin Reprod Endocrinol* 1983;1:1,41-52. 5. Barnes RB, Roy S, Lobo RA: Comparison of lipid and androgen levels after conjugated estrogen or depo-medroxyprogesterone acetate treatment in postmenopausal women. *Obstet Gynecol* 1985;66:216-219.

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EDITORIALS

Home Care Prescription Drug Reimbursement

The latest Hoffmann-La Roche Public Issue Report deals with home health care and getting the most out of the Medicare dollar. The title is "Home Care Prescription Drug Reimbursement: A Case for Intravenous Antibiotics."

The report discusses and rationalizes the growth and importance of home health care. The Appendix to the booklet lists 44 services and products that are common to both hospital and home care.

According to the report, "Medicare will now cover home intravenous chemotherapy agents and supplies when administered by means of an electronic infusion device. Although home intravenous antibiotics therapy has many similarities (including the need for precise dosing), the Health Care Financing Administration has recently denied coverage of home intravenous antibiotic therapy. This policy is based on a bureau decision that the scientific literature is insufficient to demonstrate that the administration of intravenous antibiotic therapy is safe and effective in the home."

One study showed that it cost $243.22 per day in the hospital but only $69.35 per day for antibiotics at home. Another report stated that an average of $1,600 per patient was saved by home antibiotics administered to a group of 15 patients.

Medical care in the home is increasing at a tremendous rate. Cost savings without any loss of effectiveness is characteristic of all published reports. This 28-page booklet contains a full and ample discussion of the problem and its partial cure. See your Roche representative for a copy.

Two Helping Questions

Commentary

Some time ago I started using two questions when trying to decide what I was looking at, on a patient's x-ray films.

They are, when trying to decide if an image is the spleen, for example:

1. If this isn't the spleen, what is it?
2. If this isn't the spleen, where is the spleen?

Often, both of these questions can be reduced to an absurdity, and I find myself convinced of the truth of my initial impression and can go on to other matters, feeling more comfortable about the first impression.

Of course this technique of reducing alternative diagnoses to an absurdity can be used with other problems.—R.J. Noveroske, M.D., Newburgh

Good News: Four Killer-Cancers Now Can Be Prevented or Cured

The cure of cancer is making giant steps forward. Four of the most common killer-cancers may now, with the proper measures, be either almost entirely prevented or be diagnosed early enough to insure an almost 100% cure rate.

The Pap smear has contributed one of the most effective early diagnostic tests for carcinoma of the cervix. If this test is universally adopted and performed in the proper manner, and is followed by adequate treatment, carcinoma of the cervix will be almost entirely eliminated as a cause of death.

Mammography is highly diagnostic and is becoming possible with less and less radiation. If its use becomes universal and the proper treatment is applied at an early stage, the cure rate for carcinoma of the breast will, in all probability, be almost 100%.

If everyone, above a certain age, is screened regularly for occult blood in the stool specimen, and if proper diagnostic procedures are performed to rule out cancer of the colon and rectum, or to locate a large bowel cancer, such diagnoses will, for the most part, be made in time to cure the cancer.

Such screening procedures are comparatively easy to accomplish. They are not overly expensive. Their use in patients should be universal. To be accepted by everyone and to be performed at the correct intervals and at the recommended ages will require patient compliance of a high order.

This is where public education comes in. The most important event in everyone's life from now on should be the acquisition of reliable information on cancer and the formation of a will to follow the steps to achieve cures.

When such a program is established and followed carefully, the number of cures will be astonishing.

Public education is also needed in the latest findings concerning the prevention of cancer of the colon by dietary changes.

If tobacco is eventually outlawed, cancer of the lung will almost disappear. Cure of this cancer has been practically impossible. Prevention is the big word here.

We are now living in a span of history in which prevention of some cancers and the early diagnosis and prompt treatment of others is possible. All that is needed is to let everyone know of the good news.

Teens: Sexually Active But Sexually Illiterate

The Planned Parenthood Federation has announced the results of a nationwide poll conducted by Louis Harris & Associates on teenagers' views on sex, pregnancy and birth control.

No wonder there are so many teen pregnancies. More than half of teenagers are sexually active by age 17 and only one-third of them use contraceptives consistently. This is characterized as "sexually active but sexually illiterate."

The "reason" is thought to be a result of most teenagers' impression that all sexual activity is spontaneous, unplanned and just happens. And further that this situation is all right but that planning is all wrong.

The report states: "This idea is not only preposterous, it is extremely dangerous. And until we create a social climate in which sex is spoken about in clear and open terms, and people are able to acknowledge that they are going to have sex, we will continue to see the disastrous consequences that we are seeing today."

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Alfrieda Mackel (Mrs. Frederick)
ISMA Auxiliary President 1986-87

Suzanne Miller, editor of *The Pulse*, gathered these pictures to "capture some of the moments in this Auxiliary year." The idea is to show the vital and enthusiastic support that the Auxiliary offers the medical profession. That support is perhaps best depicted by the slogan shown at the bottom left corner of the Auxiliary tote bag, "Doctors' Wives Care."

(*The Pulse*, published in March, July, September and December, features informative articles on AMA-ERF activities, legislation, health and membership. Each issue includes a message from the state Auxiliary president.)



Edi Spellmeyer (left), Wayne-Union County legislative chairman, receives her Program Book from chairman and editor Phyllis Poehler.



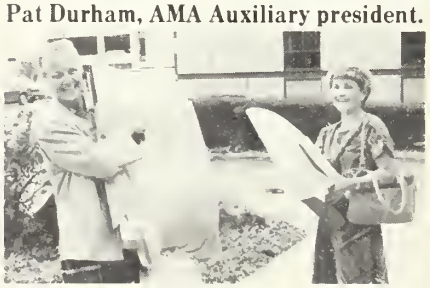
Attending last year's Leadership Conference were Allen County auxilians (from left) Carolyn Kachmann, Janet Thompson and Joanne Juergens.



Each Indiana delegate to the National Convention carries a black-and-white tote bag filled with notes and materials gathered during the convention. The bags are embellished with tokens traded with other auxilians across the country.



Rod Ashley of Grant County talks male spouse membership recruitment with Pat Durham, AMA Auxiliary president.



In need of a stronger bag are Josette Rolley (left) and Andrea Kuipers, AMA-ERF chairmen.



Alfrieda Mackel, Auxiliary president, talks with Dr. John J. Coury Jr., AMA president, at the Fort Wayne Museum of Art.



Trudy Urgena (left) and Pat Mohler register participants at the September Leadership Conference.



Anne Schuster, legislative chairman, addresses an Auxiliary legislative session.

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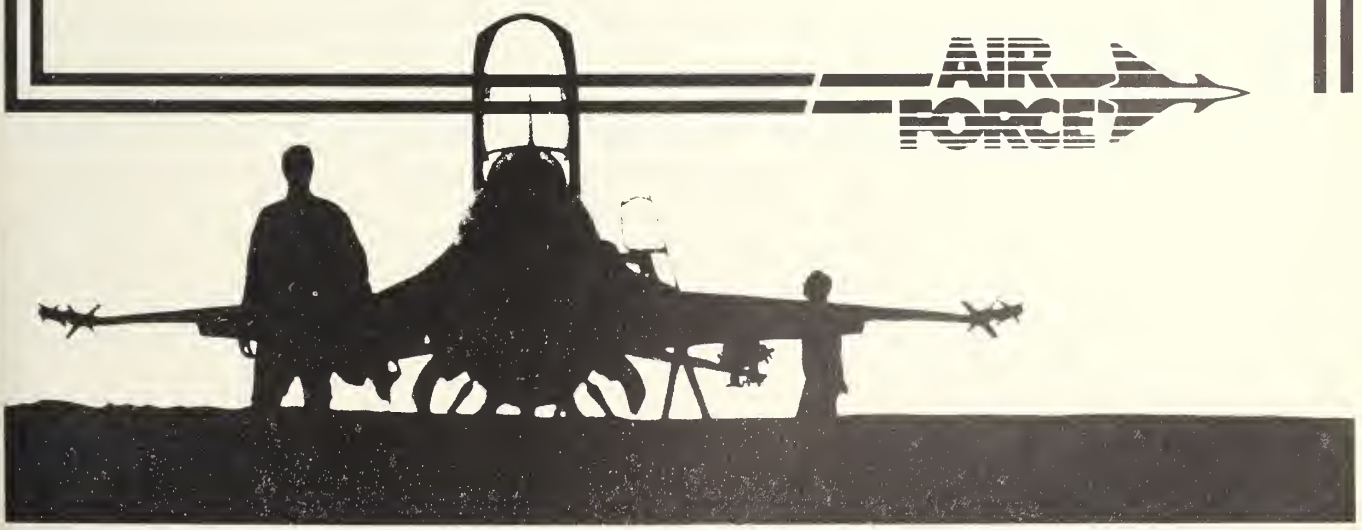
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All diplomates of the ISMA are invited to enter a professional card in the *Directory*.

NEWS NOTES

For the Asking . . .

• The special concerns of medical families are highlighted in a series of booklets being published by the AMA Auxiliary. The series is entitled, "What Every Physician's Spouse Should Know," and features topics such as impairment, professional liability, medical marriage, and retirement and estate planning. The cost for all booklets in this series is $5 per copy. Orders are to be prepaid and sent to AMA Auxiliary, 535 N. Dearborn St., Chicago 60610.

• Paget's disease of bone is the subject of a new educational booklet for physicians. Free copies of the booklet are available from Norwich Eaton Pharmaceuticals medical and hospital sales representatives or from the Norwich Eaton Marketing Department, 17 Eaton Ave., Norwich, N.Y. 13815.

• "The Physician's Advisory" (December 1986 issue) contains a news story about a decision by a California appellate court that held the physician responsible for patient discharge even though he had followed a Medicaid determination. The decision is described as a lesson for all doctors, that is, fight for the patient's authorized care or face possible malpractice liability. The annual subscription price for the newsletter, published monthly, is $120. Individual issues are $15 each. The newsletter is published by a group of attorneys who review business and legal difficulties that occur in the U.S. and then discuss their consequences. The address is MCA Publications, P.O. Box 126, Bala Cynwyd, Pa. 19004.

• The Hearing Industries Association (HIA) is offering physicians a free flip chart designed to help doctors educate patients about hearing loss and encourage hearing aid use. The flip chart features an overview of the causes of hearing loss and the types of hearing aids available; it includes actual-size color photos of each hearing aid and comes with a patient brochure on hearing impairment. For a free flip chart and 25 brochures, contact Carole Rogin, HIA, 1255 Twenty-Third St., N.W., Washington, D.C. 20037—(202) 833-1411.

• Copies of the November 1986 issue of "Laboratory Medicine," devoted to the topic of acquired immunodeficiency syndrome (AIDS), may be ordered from the publisher, the American Society of Clinical Pathologists, 2100 W. Harrison St., Chicago 60612. The special issue summarizes the most recent knowledge on the epidemiology, etiology, clinical presentations, laboratory abnormalities and laboratory precautions associated with AIDS.

• "The AIDS RECORD," the first national newsletter to provide AIDS epidemic news, current data and resource contacts for professionals, has begun twice-a-month publication. The charter rate for 24 issues is $275. The address is: BIO-DATA Publishers, P.O. Box 66020, Washington, D.C. 20035.

• "Answers about AIDS" is the title of a 54-page pamphlet published by the American Council on Science and Health. It contains a full discussion of the disease and its risks and preventions for both heterosexual and homosexual individuals. For a copy, send a SASE (#10, 66¢ postage) to AIDS Report, ACSH, 47 Maple St., Summit, N.J. 07901.

New Drug Available to Treat Severe Recalcitrant Psoriasis

The availability in the United States of a new prescription drug to treat severe recalcitrant psoriasis—a serious and sometimes life-threatening skin disease—was announced in December at the annual meeting of the American Academy of Dermatology.

The product, Tegison® (etretinate/Roche), was developed by Hoffmann-La Roche Inc. of Nutley, New Jersey, and will be marketed by Roche Laboratories, the company's pharmaceutical division.

Tegison, a derivative of vitamin A known as a retinoid, is indicated for the treatment of severe recalcitrant psoriasis, including the erythrodermic and generalized pustular types. This new medication should be used only by patients who have been unresponsive to or intolerant of standard treatments for severe psoriasis: topical corticosteroids, oral corticosteroids, exposure to ultraviolet light and methotrexate.

Studies indicate that significant adverse effects can occur with Tegison therapy. Therefore, Roche recommends special measures be taken with its use, including that Tegison be prescribed only by physicians knowledgeable in the systemic use of retinoids, and that special attention be given to patient selection and monitoring.

In particular, Tegison is known to cause severe birth defects. It should not be used by women who are pregnant, who intend to become pregnant, or who are unreliable or may not use reliable contraception while undergoing treatment. The period of time during which pregnancy must be avoided after treatment is concluded has not been determined. Other side effects, such as elevation of blood lipids, are potentially serious, as are benign intracranial hypertension and hepatitis. In clinical trials, many patients showed evidence of hypertoses.

Sex Ed in Schools Touted as Way to Curb AIDS

The American Academy of Family Physicians is taking a strong stand in support of the campaign against AIDS advanced by Surgeon General C. Everett Koop.

Dr. Koop recommends comprehensive education in human sexuality at grade levels as low as elementary schools. On the air Dr. Koop has said that he thinks this might be as early as the third grade.

The Academy president, Dr. Robert H. Taylor, has said: "AIDS is taking us quickly beyond waiting until our children are in high school or beyond to teach the fundamentals of human sexuality, its hazards as well as its joys."

COBRA: The New Patient Transfer Law Whose Bite Is Worse Than Its Bark

Most hospital transfers of emergency patients in the country in the last few months have been in violation of a new federal law, according to Stephen A. Frew, an attorney and national speaker on medical/legal issues. Most physicians are not yet aware of the law, Frew said.

The law, Section 1867 of a law known as COBRA, sets up federal standards for examination, stabilization and transfer of emergency patients and women in labor.

Aimed at preventing "dumping" of undesirable cases and patients without insurance, the new law sets severe penalties for hospitals and physicians who violate the procedures, according to Frew.

Among the risks are $25,000 fines, loss of all hospital Medicare reimbursement permanently or for a suspension period, and civil suits, he said.

Copies of Section 1867 and a report covering its interpretation and impact on emergency medicine, EMS, and HEMS are available from Frew's office. There is a $1.00 charge per copy for postage and distribution costs. Requests should be addressed to: Stephen A. Frew, Box 969, Rockford, Ill. 61105.

Digital Technology Seen as Aid in Health Care Record-Keeping

The technology of being able to store information on optical disks is seen as a major step in the efforts of large hospitals to computerize storage of x-ray images and other patient records.

Billing data and medical histories have for years been stored on conventional magnetic disk or tape systems because the numbers and words in the records can be easily put into the computer through conventional keyboards. But x-ray images and other non-alphanumeric information has required development of digital retrieval and storage equipment that allows the information to be put on optical disks with laser film scanners.

Such devices are just beginning to be used in U.S. hospitals, primarily in continuing clinical research to assess the steps required to convert entire radiology departments to digital storage of x-ray images and other radiological procedure data.

The workload is huge. There are currently about 23,000 x-ray machines in operation in the United States, taking about 300 million films per year, according to Mitsubishi Electric Sales America, Inc.

CME Quiz Answers

Although this issue of INDIANA MEDICINE does not feature the monthly Indiana University School of Medicine CME article, the series will resume next month.

Following are the answers to the January 1986 CME article, "Fluid and Electrolyte Disturbances in the Perioperative Period," by Craig M. Stoops, M.D.

1. c
2. c
3. d
4. b
5. c
6. a
7. b
8. b
9. e

Indiana Air Separation Plant Is America's Largest

Airco, a leader in industrial gas production and technology, has opened the largest air separation facility ever built in the United States. It is located in Springville, Ind., mid-way between South Bend and Chicago.

The plant will produce 1,000 tons per day of nitrogen, oxygen and argon in liquid form. Airco is able to measure gas purity to within 0.1 ppm. The firm also has plants for the recovery of helium, carbon dioxide and hydrogen.

Physician Recognition Awards

The following ISMA physicians are recent recipients of the AMA's Physician Recognition Award. This award is official documentation of Continuing Medical Education hours earned, and is acceptable proof in most states requiring CME in re-registration that the mandatory hours of CME have been accomplished.

Akin, Daniel P., New Albany
Allegretti, Michael L., Munster
Armbuster, Thomas G., Fort Wayne
Cobb, Clarence M., Indianapolis
Conard, Douglas S., Frankfort
Coons, Philip M., Indianapolis
Custodio, Camia A., Merrillville
Gammell, Lindley L., Columbus
Heck, Larry L., Indianapolis
Ignacio, D.G., Richmond
Kamen, Jack M., Gary
Kaminsky, Marc E., Fort Wayne
Kunz, Robert J., Lebanon
Melchior, Jerome E., Vincennes
Meyer, Claude J., Sellersburg
Moore, Jeffrey K., Evansville
Pairitz, Frank D., South Bend
Rahman, Sheikh A., Lawrenceburg
Seibel, Robert M., Nashville
Tate, Michael M., New Albany
Tierney, William J., Anderson
Wagner, Lindley H., Lafayette

NEWS NOTES

Here and There . . .

Dr. Steven R. Smith of Indianapolis has been named Indiana Bell's medical director.

Dr. John W. Harley of Goshen has been named a fellow of the American College of Surgeons.

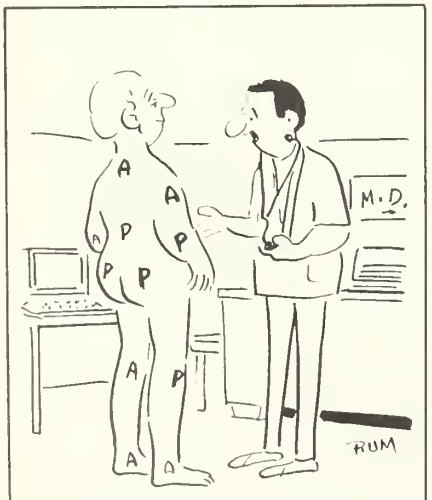
Dr. John E. Schreiner, a Bremen family physician 38 years, has retired from practice; the town's board of trustees proclaimed Nov. 23 "Doc Schreiner Day."

Dr. Windham Bremer of Michigan City is the new president of the medical staff at St. Anthony Hospital; Dr. Mirza Raheem is vice-president, and Dr. Thomas Roberts is secretary-treasurer.

Dr. Phyllis A. Grant has been named "New Castle Woman of the Year" by the Women's Division of the New Castle Area Chamber of Commerce.

Dr. Kenneth R. Woolling, an Indianapolis cardiologist, has retired after 43 years in practice.

Dr. Ronald C. Hamaker of Indianapolis was a guest faculty member at a recent course on "Facial Reconstructive Surgery," co-sponsored by the Ohio State University Dept. of Otolaryngology and the American Academy of Facial Plastic and Reconstructive Surgery; in November, he addressed the Louisville Otolaryngology-Head and Neck Surgery Society on "Intraoperative Radiation Surgery."



"I appreciate your efforts to pin-point your aches and pains."

Dr. J. William Wright Jr. of Indianapolis has been elected vice-president of the American Academy of Otolaryngology-Head and Neck Surgery.

Dr. Mohammad Arab of LaPorte has been elected to fellowship in the American College of Surgeons.

Dr. E. Henry Lamkin Jr. of Indianapolis has been re-elected president of the medical staff, Methodist Hospital of Indiana; also re-elected were Dr. Charles B. Carter, vice-president, and Dr. Richard F. Graffis, secretary-treasurer.

Dr. Randolph W. Lievertz of Indianapolis discussed menopause as part of a November CME program at Reid Memorial Hospital, Richmond; also in November, he presented two lectures on the medical effects of alcohol to Marion County probation officers.

Dr. Louie O. Dayson of Vincennes discussed heart-related concerns during a December workshop at the local YMCA.

Radiologists at UCLA Med Center Converting X-rays to Video Display

Within 10 years, officials at UCLA Medical Center in Los Angeles hope that x-ray images will no longer be stored on film.

The medical center has embarked on a program to convert its entire Department of Radiological Sciences to digital storage of x-ray and other medical images. The conversion will not only eliminate the problem of filing some 500,000 medical images a year, but it will also enable physicians working in any part of the huge, 700-bed teaching hospital to have quicker access to medical images of their patients by being able to call them up on video monitors.

With digital storage, medical images are converted directly into electronic signals that are stored on laser disks. As part of that program, the Mitsubishi Medical Image Work Station has been installed to both store the images and allow the examination of medical images which require the highest possible resolution for precise diagnosis.

Dr. Rose S. Fife, a staff rheumatologist at the I.U. Medical Center, has been named a member of the board of directors, Indiana Chapter of the Arthritis Foundation.

Dr. Ned B. Hornback, chairman of the Dept. of Radiation Oncology, I.U. School of Medicine, was an invited lecturer at the November Plenary Session of the National Japanese Hyperthermia Society Conference in Osaka.

Dr. Richard T. Miyamoto of Indianapolis was an invited speaker at XX Pan American Congress of Otorhinolaryngology-Head and Neck Surgery, Puerto Vallarta, Mexico in November; he spoke on "Cochlear Implants in Children" and participated in a panel discussion on "Surgery of the Middle Cranial Fossa Floor."

Dr. Louis F. Romain of Fort Wayne was guest speaker at the November meeting of the local Parkinson's Support Group.

Dr. Panayotis Iatridas of Gary discussed psychiatric disorders during the December meeting of the Manic Depressive and Depressive Association of Northwest Indiana.

Dr. John F. Ling, a Richmond internist who most recently served as physician for the Wayne County jail and county adult health clinics, has retired.

Dr. C. Jules Heritier of Columbia City, who practiced as a family physician in Whitley County 40 years, has retired.



"I've come back to you for a second opinion. I wasn't listening the first time."

Dr. Charles H. Caylor, president of the Caylor-Nickel Medical Center in Bluffton, has been named to the board of directors, Indiana Chamber of Commerce.

Dr. Dean Maglinte of Indianapolis was on the panel of discussants on Major Events in Radiology 1986 during the Scientific Assembly and Annual Meeting of the Radiologic Society of North America, held in Chicago in December.

Dr. Timothy R. Tanselle of Crawfordsville discussed the doctor-patient relationship during a November Evening of Health lecture at Culver Union Hospital.

Dr. C.J. Ottinger, a Fort Wayne neurologist, addressed the November meeting of the local Amyotrophic Lateral Sclerosis Support Group.

Dr. C. William Hanke of Indianapolis is president-elect of the Indiana Division, American Cancer Society.

Dr. Ben H. Park of Lebanon is the new chief of the medical staff at Witham Memorial Hospital.

AMSA Announces New Plan for Health Education Assistance Loans

The American Medical Student Association (AMSA) has announced the inauguration of a new assured access plan to make Health Education Assistance Loans (HEAL) available through its foundation at a significantly reduced cost to its more than 37,000 medical and osteopathic student-members.

The AMSA "HEAL Deal" is being offered in partnership with the Key Bank of Central Maine, Knight Tuition Payment Plans Inc., and the Student Loan Marketing Association (Sallie Mae).

The new AMSA plan is designed to assure student-members across the country of a lower cost of financing on HEAL loans—a major federally sponsored loan program for health professions students—by offering below market interest rates on the loans while borrowers are in school or in residency or internship programs. The plan also offers borrowers a choice of payment options during the in-school, residency or internship period and an interest rate cap, or ceiling, throughout the life of the loan, potentially to further reduce the cost of financing.

ACEP Unhappy with Safety Commission's ATV Decision

The American College of Emergency Physicians has expressed "disappointment" with the Consumer Protection Safety Commission (CPSC) for its weak response to the dangers of the all-terrain recreation vehicles (ATVs).

The CPSC rejected the recommendations of its own ATV Task Force and instead called only for "voluntary standards" for limiting the sale of ATVs intended for use by small children. The ACEP had recommended removing from the market all ATVs designed for children below the age of 12.

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Consents and Guidelines:
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Ambulatory Surgery and Anesthesia Guidelines
Policies and Procedures for Patient Care

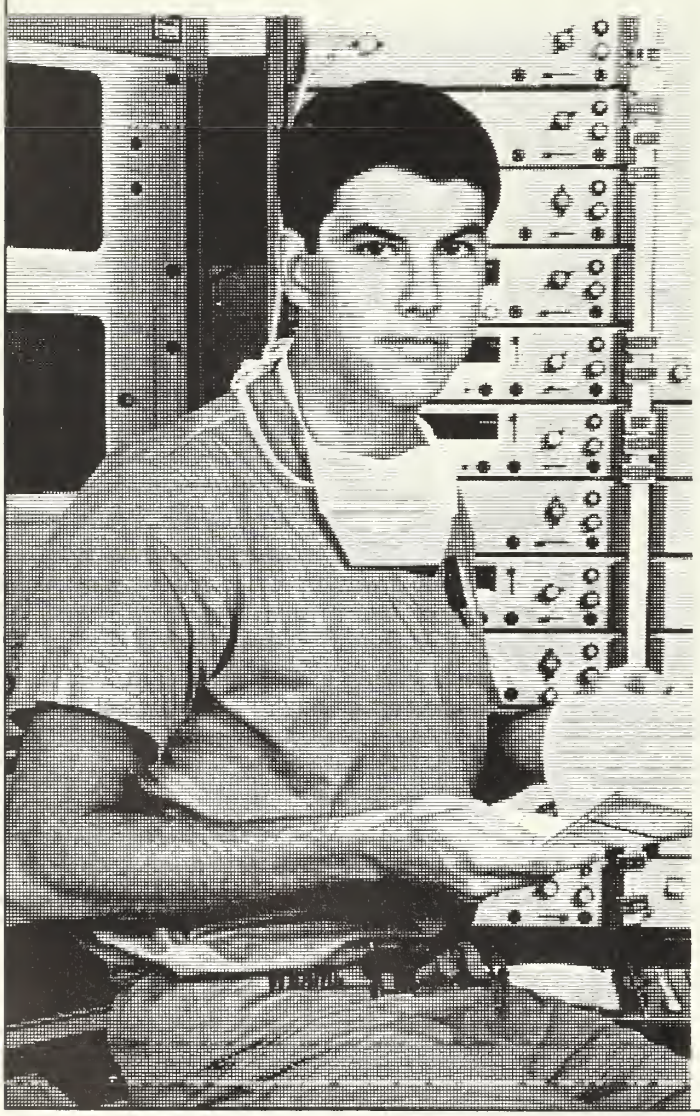
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OBITUARIES

Leland J. Mortenson, M.D.

Dr. Mortenson, 89, a retired Fort Wayne general practitioner, died Nov. 1 at his home.

He was a 1941 graduate of the University of Illinois College of Medicine.

Dr. Mortenson, who retired from practice in 1976, was a member of the American Academy of Family Physicians. He was president of the medical staff at Lutheran Hospital during the mid-1950s.

Donaldo E. Lacera, M.D.

Dr. Lacera, 56, a Hammond pathologist, died Oct. 24 at his home in Flossmoor, Ill.

He earned his M.D. degree in 1957 from the University of Cartagena, Columbia, South America.

Dr. Lacera, a diplomate of the American Board of Pathology, was director of laboratory services at Community Hospital in Munster. He also was president of Associated Pathologists in Munster and a consulting pathologist at St. Margaret Hospital in Hammond.

A. Donald Merritt, M.D.

Dr. Merritt, 61, a former Indianapolis physician who founded the Dept. of Medical Genetics at the I.U. School of Medicine, died Nov. 25 in Bethesda, M.D.

He was a 1952 graduate of George Washington University School of Medicine and was a veteran of World War II.

Dr. Merritt was chief of the Health Professions Applications Branch of the National Library of Medicine from 1979 until his retirement in 1984. He was certified by the American Board of Internal Medicine and was a fellow of the American College of Physicians.

Joseph Goldstone, M.D.

Dr. Goldstone, 87, a retired Gary surgeon, died Aug, 23, 1986.

He was a 1923 graduate of the University of Nebraska College of Medicine.

Dr. Goldstone was a member of the International Academy of Proctology and a member of the ISMA Fifty Year Club. He had lived in Florida since retiring from practice.

Herbert E. Baumeister, M.D.

Dr. Baumeister, 66, a retired Indianapolis anesthesiologist, died Nov. 12 at Methodist Hospital.

He was a 1950 graduate of Indiana University School of Medicine and was an Army veteran of World War II.

Dr. Baumeister, who retired from practice last year, had practiced at Winona Hospital 20 years. He was a member of the American Society of Anesthesiologists and the International Anesthesia Research Society, and was a former president of the Indianapolis Society of Anesthesiologists.

Wallace E. Childs, M.D.

Dr. Childs, 77, a retired Madison radiologist, died Oct. 18 at King's Daughters' Hospital.

He was a 1936 graduate of Indiana University School of Medicine and served with the Army-Air Forces in World War II.

Dr. Childs joined the staff of King's Daughters' Hospital in 1949 and served there until he retired in 1973. He also was a radiologist at Madison State Hospital for 20 years. He was a former president of the Jefferson-Switzerland County Medical Society, was a diplomate of the American Board of Radiology, and was a fellow of the American College of Radiology.

John F. Rigg, M.D.

Dr. Rigg, 93, a retired Indianapolis general practitioner, died Nov. 15 at his home in North Palm Beach, Fla.

He was a 1920 graduate of Indiana University School of Medicine and an Army veteran of World War I.

Dr. Rigg practiced in Indianapolis from 1920 to 1959. From then until he retired 10 years later he was a clinician for the Dade County (Fla.) Health Department. He was a diplomate of the American Academy of Family Practice and a member of the ISMA Fifty Year Club.

Robert W. King, M.D.

Dr. King, 69, a Cedar Lake general practitioner, died Oct. 18 at St. Anthony Medical Center, Crown Point.

He was a 1944 graduate of the Loyola University Stritch School of Medicine, and was a veteran of World War II and the Korean War.

Dr. King was credited with getting Cedar Lake incorporated in 1967. He served one term as a town trustee. He was a member of the Board of Governors of four local hospitals.

Memorials: Indiana Medical Foundation

The Indiana Medical Foundation, Inc. was formed by the Indiana State Medical Association "for religious, charitable, scientific, literary or educational purposes." It provides financial assistance to support the educational mission of INDIANA MEDICINE.

Contributions made to the Foundation are deductible by donors in accordance with the Internal Revenue Code. Gifts are deductible for Federal estate and gift tax purposes.

The Foundation is pleased to acknowledge the receipt of gifts in remembrance of the following individuals:

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COMMERCIAL ANNOUNCEMENTS

ATTENTION—Job openings available nationwide for Board eligible/certified physicians: Anesthesiology, Dermatology, Emergency Medicine, General Practice, Internal Medicine, Nuclear Medicine, OB-GYN, Orthopedic Surgery, Psychiatry and Radiology. Positions available for other specialties. Call (317) 848-2005, Jeffrey Bocock, ADM., Hunter-Lawyer Medical.

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EMERGENCY MEDICINE Position Available: Opportunity for experienced Emergency Physician to work weeknights 6 p.m. to 8 a.m., Kendallville, Ind. Contact Mr. John F. Ling Jr., Administrator—(219) 347-1100, ext. 120.

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EMERGENCY PHYSICIANS NEEDED, Chicago, Illinois. Full or part time. Prefer Board-certified in emergency medicine or Board-eligible, or at least three years full time experience. New contractual situation with new group will offer outstanding growth possibilities and excellent compensation. Take advantage of this exciting opportunity to live and work in dynamic Chicago. Send resume as soon as possible to Kathleen Babe, 9401 S. Sacramento, Evergreen Park, Illinois 60642, or call Kathleen Babe, (312) 425-7797. Please don't delay in responding to this wonderful opportunity as there are only four positions available.

MEDICAL EQUIPMENT—**50% off** previously owned medical, laboratory, office, x-ray, ultrasound equipment in excellent condition. We buy, sell, broker and repair. Appraisals by certified surgical consultants. Ask about our Holter Scanning Services. Medical Equipment Resale, Inc., 24026 Haggerty Road, Farmington Hills, Michigan 48018—(313) 477-6880. Call anytime.

INDIANA—Physician needed. New walk-in medical facility. Guaranteed salary, fee-for-service incentives, regular hours. Please reply to P.O. Box 1631, Marion, IN 46952.

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In short, make sure you do what your mother always told you to do. Eat your vegetables.

AMERICAN CANCER SOCIETY

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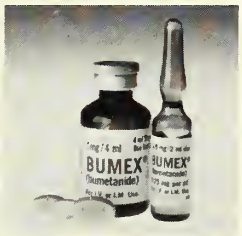
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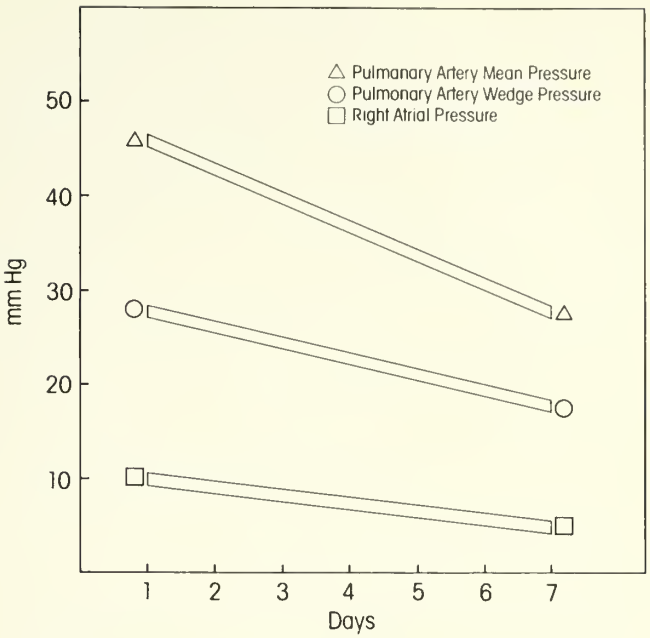
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References: **1.** Olesen KH, *et al Postgrad Med J 51* (Suppl 6) 54-63, 1975 **2.** Hondler B, Dhingra RC, Rosen KM *J Clin Pharmacol 21* 706-711, Nov-Dec 1981 **3.** Brater DC, *et al Clin Pharmacol Ther 34* 207-213, Aug 1983 **4.** Brater DC, Fox WR, Chennovosin P *J Clin Pharmacol 21* 599-603, Nov-Dec 1981 **5.** Davies DL, *et al Clin Pharmacol Ther 15* 141-155, Feb 1974

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Prevention of hypokalemia requires particular attention in patients receiving digitalis and diuretics for congestive heart failure, hepatic cirrhosis and ascites, states of aldosterone excess with normal renal function, potassium-losing nephropathy, certain diarrheal states, or other states where hypokalemia is thought to represent particular added risks to the patients
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Possibility of effect on glucose metabolism exists Periodic determinations of blood sugar should be done, particularly in patients with diabetes or suspected latent diabetes
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Especially in presence of impaired renal function, use of parenterally administered Bumex should be avoided in patients to whom aminoglycoside antibiotics are also being given, except in life-threatening conditions
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Interaction studies in humans have shown Bumex to have no effect on warfarin metabolism or on plasma prothrombin activity
Pregnancy Bumex should be given to a pregnant woman only if the potential benefit justifies the potential risk to the fetus
Bumetanide may be excreted in breast milk
Pediatric Use Safety and effectiveness below age 18 not established
ADVERSE REACTIONS: Muscle cramps, dizziness, hypotension, headache and nausea, and encephalopathy (in patients with preexisting liver disease).
Less frequent clinical adverse reactions are weakness, impaired hearing, rash, pruritus, hives, electrocardiogram changes, abdominal pain, arthritic pain, musculoskeletal pain and vomiting
Other clinical adverse reactions are vertigo, chest pain, ear discomfort, fatigue, dehydration, sweating, hyperventilation, dry mouth, upset stomach, renal failure, asterixis, itching, nipple tenderness, diarrhea, premature ejaculation and difficulty maintaining an erection
Laboratory abnormalities reported are hyperuricemia, azotemia, hyperglycemia, increased serum creatinine, hypochloremia, hypokalemia, hyponatremia, and variations in CO_2 content, bicarbonate, phosphorus and calcium Although manifestations of the pharmacologic action of Bumex, these conditions may become more pronounced by intensive therapy
Diuresis induced by Bumex may also rarely be accompanied by changes in LDH, total serum bilirubin, serum proteins, SGOT, SGPT, alkaline phosphatase, cholesterol, creatinine clearance, deviations in hemoglobin, prothrombin time, hematocrit, platelet counts and differential counts
Increases in urinary glucose and urinary protein have also been seen
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Oral Administration. The usual total daily dosage is 0.5 to 2.0 mg and in most patients is given as a single dose
Parenteral Administration Administer to patients (IV or IM) with GI absorption problem or who cannot take oral The usual initial dose is 0.5 to 1 mg given over 1 to 2 minutes If insufficient response, a second or third dose may be given at 2 to 3 hour intervals up to a maximum of 10 mg a day
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Please see references and summary of product information on preceding page.

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MARCH 1987 VOL. 80 NO. 3

INDIANA MEDICINE

The Journal of the Indiana State Medical Association

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- **CME: Myasthenia Gravis**
- **Anti-Arrhythmic Agents**
- **The Faith Assembly**
- **Hyperbaric Medicine**
- **The Complete Physician**
  Is the Goal Worth Striving for?
- **The 'Vietnamese Time Bomb'**
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INDIANA MEDICINE

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MARCH 1987

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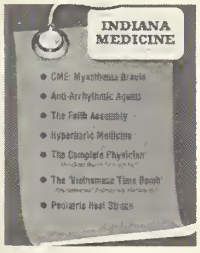
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ABOUT THE COVER

As you can see, we have several articles in this issue that we consider noteworthy. Of particular interest to nearly all of our readers, however, will be "The Complete Physician: Is the Goal Worth Striving For?" by the late Dr. Paul S. Rhoads of Richmond, Ind., Professor Emeritus of Medicine, Northwestern University.

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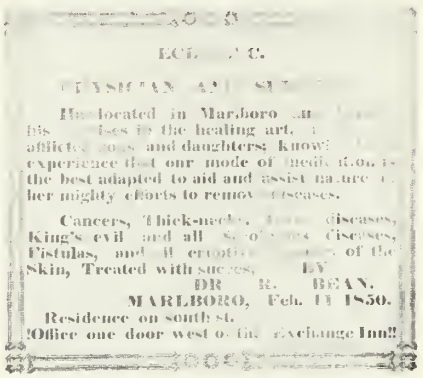
CHARLES A. BONSETT, M.D., Indianapolis

THE ADVERTISEMENT shown here was found in a turn-of-the-century record book containing the donor's names and titles of the publications donated to the Bobbs medical library wing of the St. Clair Street Indianapolis Public Library.

This record book was given to the medical museum several months ago at the time discussions were initially underway to permit the ultimate transfer of the Dr. John Stough Bobbs memorial by Gutzon Borglum to the new medical library now under construction at the Indiana University Medical Center.

The advertisement refers to a physician who was trained in the Eclectic school who was opening an office in the town of Marlboro (presumably in New York or one of the New England states). Physicians of the "regular school" (Allopaths) did not take kindly to those brethren who practiced in unconventional ways, and the Eclectics were regarded as unconventional. Another such school was the Botanics.

This page of Notes is an abbreviated version of a letter written by a Botanic student and published in the *Locomotive* on page 3 of the Feb. 8, 1851 issue of this early Indiana newspaper. The student, David J. Lee, had made an unsuccessful attempt to enroll in the anatomy class of Professor Meeker of the Indiana Central Medical College, and his letter credits Dr. John Bobbs as the ultimate cause of this frustrated effort.



ECL[illegible] C.

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Has located in Marlboro [illegible] his services in the healing art. [illegible] afflicted sons and daughters: Know[illegible] experience that our mode of medic[illegible] is the best adapted to aid and assist nature [illegible] her mighty efforts to remove diseases.

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DR R. BEAN.

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Residence on south st.

Office one door west of [illegible] Exchange Inn!!

This 137-year-old newspaper ad was placed by an Eclectic physician. Such practitioners were regarded by "regular school" physicians as "unconventional."

Medical College Outrage

Mr. Locomotive: It was doubtless understood when the Indiana Central Medical College was founded that anyone of good moral character, and who was willing to conform to its regulations, could procure admission to its lectures, whatever might be his private opinions with respect to the different systems of medicine. Such at least is the custom all over our land . . . In view of these facts, let the following circumstances be considered in regard to law and justice, then let the public decide if these things are right.

About the first of last month (January) I procured from Professor Meeker his ticket to attend lectures on anatomy for the balance of the course. The only question he asked was whether I was a student of medicine, not whether Dr. Abbott (a Botanic) was my preceptor, nor if I intended to be a "steam doctor;" nothing of the kind was mentioned. I paid him for the ticket and attended lectures for about three weeks. Nothing was said about the matriculation fee, nor did I know anything about it. As soon as it became known that I was not reading with an Allopathic physician . . . the students began their insults, hissing, and hollering "steam" and "yarbs" (herbs), not only in the College but on the streets . . . They caucussed and passed resolutions declaring that I should leave the class . . . These were presented to the faculty . . . Professor Meeker . . . declared that I had violated none of the rules of the College, that I had a right to come and learn . . . even though I doctored with cornstalks. . . . The faculty deliberated, and the next day, on my way to lecture, the following note was handed me:

Mr. Lee, Sir,

At a meeting of the faculty of the Indiana Central Medical College held this day, the following resolution was adopted:

Resolved: That in conformity with the usage of this College, Mr. Lee is not a regularly matriculated student and cannot become a member of the class without.

If Mr. Lee will return his ticket to Professor Meeker or the Dean, the price paid therefor will be refunded. It is hoped Mr. Lee will understand that the harmony of the class renders this step necessary.

(signed) J.S. Bobbs
Dean of the Faculty

The above note was shown to . . . a trustee of the institution . . . by whose advice I proceeded to the College. Meeting with the Dean on my way, he offered to refund my money but positively forbad my attending the lectures should even all the trustees in the city demand it. I presented my ticket but was refused admission by the janitor under the instruction of the Dean . . . The reason for (this) . . . was that Dr. Abbott was my preceptor and I did not hail from the "regular army."

I am aware that the lectures were an advantage to me in the pursuit of my studies; they are doubtless of first order . . . But if my character as a physician is to be based upon connection with such an institution after such proceedings as these . . . tell it not in Indiana that I have ever been there . . .

In justice I would say that a majority of the students and several of the professors have acted as become gentlemen, and disapproved of the treatment I have received . . . The public (will) . . . judge whether (the) oft repeated assertion that Botanic physicians are ignorant of the medical sciences is correct (or not).

February 1, 1851
David J. Lee

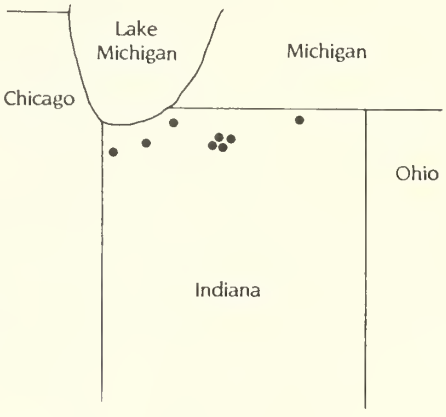
No response to Mr. Lee's letter appeared in subsequent issues of the *Locomotive*. It would be of interest to know what ultimately happened to his career.

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Meridian has prepared a referral information kit detailing our facilities and services. In it you will find information on how you and your patients' families in the northern Indiana areas served by our eight facilities can take advantage of the many nursing care programs that we offer. This kit is available, without charge, to physicians and hospital administrations. To obtain a copy for your office, please clip and send the coupon below.

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WHAT'S NEW?

Noetic Systems announces a new line of disposable, waterproof, self-sealing cast and bandage covers. The Medipac Shower Protection Sleeve comes in four sizes, hand, arm, foot and leg. One end of the sleeve is closed; the other end is attached to the extremity by an adhesive band. The sleeves are waterproof enough to allow the patient a shower bath.

Roche is packaging Roferon® -A (Interferon Alfa-2a, recombinant/Roche) in powder form with a refrigerated storage life of up to three years. The same preparation in liquid form has a storage life of up to one year. The sterile interferon powder will be packaged in vials containing 18 million international units, with an accompanying vial containing 3 ml. of diluent.

Bristol-Myers has announced FDA approval for marketing Enkaid® (encainide hydrochloride). Enkaid is a new agent for the treatment of arrhythmias. The drug is described as an important new first-line therapy for ventricular arrhythmias. Clinical research indicates a low incidence of side effects.

Burroughs Wellcome has a new liquid dosage for Septra® Grape Suspension (trimethoprim and sulfamethoxazole) for the treatment of acute otitis media and urinary tract infections in pediatric patients. The suspension has a sorbital base which does not promote tooth decay. The pink, cherry flavored Septra Suspension will be continued. Research shows that about one-half of pediatric patients favor the cherry flavor, while the other half favor grape.

The Lawyers Co-operative Publishing Co. announces *The Law of Medical Practice in Illinois*. It is a comprehensive, single-volume, medical-legal encyclopedia addressing the specific needs for physicians practicing in Illinois. Updated by annual pocket-part supplementation and new or revised volumes or editions as required. No charge for upkeep material issued within six months of purchase shipment. Hardbound, $79.50.

The 1987 edition of *Current Award Trends* is now available from Jury Verdict Research, Inc. *Trends* reports on the size and other characteristics of personal injury verdicts. The number of million dollar verdicts has increased since 1960's five per year to 1986's nine or more per week, but the increase has declined since 1981. The increase is now less than the increase for medical costs, a major part of the P.I. awards. The 31-page nationwide report contains analyses, charts and graphs on the subject. The cost is $25.

Auburn House Publishing has a new book, *To Do No Harm: A Journey Through Medical School*. The author is Philip Reilly, J.D., M.D. It was written "for medical students, doctors, patients and those who were or will be so numbered." Topics covered include: 1.) The need for studying patients with scientific objectivity in the context of the student's own subjective, emotional involvement; 2.) Communicating with patients: What to tell and when? and 3.) Coming to terms with death and dying. Dr. Reilly is medical director of the Eunice Kennedy Shriver Center for Mental Retardation in Massachusetts. 292 pages—hardbound $24.95, paperbound $16.95.

Abbott Laboratories announces that an 11-minute videotape on the use of alpha-fetoprotein (AFP) testing for open neural tube defects is now available to physicians. The tape reviews the AFP text protocol, provides instruction regarding the interpretation of test results and features an interview with Barbara Crandall, M.D., director of prenatal diagnosis at the UCLA School of Medicine.

News of what is new in the medical supply industry is composed of abstracts from news releases by book publishers and manufacturers of pharmaceuticals, clinical laboratory supplies, instruments and surgical appliances. Each item is published as news and does not necessarily constitute an endorsement of a product or recommendation for its use by INDIANA MEDICINE or by the Indiana State Medical Association.

Amcest Corporation has a new emergency call system especially for those who live alone. PERSYS, for Personal Emergency Response System, is actuated by a pendant worn around the person's neck. A computerized message is picked up by a receiver, which may be as far away as 200 feet, and is transmitted over the phone line to the emergency communications center. The emergency operator may talk to the pendant wearer if necessary. The operator calls the police, ambulance, doctor or a friend within seconds. The operator may also be previously instructed to call relatives and a neighbor who has a key to the house or apartment. Very useful for fire alarms and for persons who might fall and break a leg and not be able to get to a phone.

General Electric Information Service has a technologic device which, through a medical office system, will transmit claims electronically to over 30 insurance companies, including the Blues. The computer, which handles reservations or billing, is not interrupted until at the end of the day. At that time the claims, which have been stored in the device, are transmitted to a central clearing house which, in turn, transmits each claim to the proper insurance company.

The C. V. Mosby Company is printing and binding a two-volume work on *The Artistry of Reconstructive Surgery*. It is edited by Burt Brent, M.D. of Stanford University and Belinda Price Bent, with 86 contributors and lithography by Robert Charles Howe. Approximately 1,000 pages in the two volumes with leather-bound cover, gilt edges, decorative end papers and slipcase. 1,700 illustrations, including 150 color plates and a limited edition of a lithograph 27″ × 27″ by Howe. $650.

Bristol-Myers has received FDA approval for marketing a new oral form of VePesid® (etoposide) for use in combination chemotherapy as first-line treatment of small cell lung cancer. It should be available to physicians in five months.



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FUTURE FILE

Rhinoplasty Seminar

A 3½-day Rhinoplasty, Nasal Aesthetic and Reconstructive Surgery Seminar will be conducted at the Hyatt Regency in Indianapolis April 2-5.

The seminar is co-sponsored by the American Academy of Facial Plastic and Reconstructive Surgery and Indiana University School of Medicine's Dept. of Otolaryngology. Dr. Stephen W. Perkins will be director of the seminar.

Participants are asked to arrange accommodations at the Canterbury Hotel (1-800-323-7500). For additional information, contact Dr. Perkins' office at (317) 849-8626.

Methodist Hospital CME

May 1: 13th Annual William Niles Wishard Jr. Memorial Lecture, Methodist Hospital, Indianapolis.

May 14-15: 22nd Annual Gordon W. and Mae Batman Lecture Series, Methodist Hospital, Indianapolis.

June 6: High Energy Fractures: External Fixation and Locking Nails, Methodist Hospital auditorium, Indianapolis.

June 24-26: 8th Annual Scientific Meeting of the American Society for the Immunology of Reproduction, Hilton-on-the-Circle, Indianapolis.

(April courses are listed in the February 1987 issue of INDIANA MEDICINE, page 130.)

For more information, contact Dixie Estridge, CME coordinator, Graduate Medical Center, Methodist Hospital of Indiana—(317) 929-3733.

Sports Fitness

The "Sports Fitness Conference and Exhibition" will be conducted April 14-16 at the O'Hare Exposition Center in Rosemont, Ill.

Pre-registration fees for one, two or three days are $90, $160 and $225. Registration at the show runs $100, $180 and $250.

For other details and to register, contact the Tower Conference Management Co., 331 W. Wesley St., Wheaton, Ill. 60187—(312) 668-8100.

St. Vincent Hospital CME

St. Vincent Hospital and Health Care Center, Indianapolis, announces the following CME programs:

April 8-10: Midas Rex Hands-on Orthopedic Workshop, Sheraton Marten House, Indianapolis.

April 25: Fifth Annual Spring Seminar in Dermatopathology; Hideko Kamino, M.D., guest lecturer; St. Vincent Hospital.

May 1-2: Seventh Annual Joseph C. Finneran Professorship, Witold J. Rudowski, M.D., Director, Dept. of Surgery, Research Institute of Hematology and Blood Transfusion, Warsaw, Poland; Cooling Auditorium, St. Vincent Hospital.

May 22: Annual "500" Orthopedic Conference, Cooling Auditorium, St. Vincent Hospital.

For more information, contact Marilyn Soltermann, CME coordinator—(317) 871-3460.

Surgery of the Hand

"Update on Surgery of the Hand and Wrist" is the subject of a 2½-day course scheduled for April 22-25 at Sead Pines, Hilton Head, S.C.

The emphasis of the course, sponsored by the American Society for Surgery of the Hand, will be on trauma and trauma-related conditions. Tuition for physicians is $450 or $500, depending on whether registration is received before or after March 25. Residents, fellows and allied health professionals are listed at $300 and $350.

For details on registration and hotels, contact the Society at 3025 Parker Road, Suite 65, Aurora, Colo. 80014—(303) 755-4588.

The *Journal of the American Medical Association* publishes a list of CME courses for the United States twice yearly. The January listing features courses offered from March through August; the July listing features courses offered from September through February.

AMA Marketing Strategies

"Marketing Strategies for Private Practice" is the topic of an AMA practice management workshop to be conducted Friday, March 27, at St. Vincent Hospital, Indianapolis.

The workshop will cover how the basic concepts of modern marketing can be applied to medical practice. For more information on registration of physicians and staff for this eight-hour workshop, please contact Carol Ann Cunningham at ISMA Headquarters.

DNA Probes

"DNA Probes in the Practice of Medicine" is the subject of an AMA conference to be held April 25-26 at the Hyatt Regency Washington Hotel on Capitol Hill.

Among the current uses of DNA are the rapid diagnosis of major viral and bacterial infections, diagnosis of genetic disorders such as Huntington's disease and muscular dystrophy, and prenatal and postnatal genetic screening.

Contact R. Mark Evans, Ph.D., Office of Biotechnology, AMA, 535 N. Dearborn, Chicago 60610—(312) 645-4567.

Child Care Conference

The 22nd Annual Indiana Multidisciplinary Child Care Conference will be held May 6 and 7 at the Union Station Holiday Inn in downtown Indianapolis.

The speakers and subjects will include: Dr. Ellen Wald—Pediatric Infectious Diseases; Dr. Jan Paradise—Pediatric Gynecology in Children and Adolescents; Drs. N. Jeffrey Maisels and Richard Schreiner—Neonatalogy; Dr. Robert Blum—Adolescent Drug and Substance Abuse; Dr. David Rothner—Pediatric Neurology; and Dr. William Weston—Pediatric Dermatology.

Contact Dr. Morris Green, I.U. School of Medicine, Riley Hospital for Children, 702 Barnhill Drive, Indianapolis 46223.

Indiana University CME

April 4-5: Advanced Trauma Life Support, Tudor Auditorium, Wishard Memorial Hospital, Indianapolis.

April 2-5: Rhinoplasty: Nasal Aesthetic and Reconstructive Surgery, Embassy Suites-Downtown, Indianapolis.

April 6-8: Update Workshop in Echocardiography, I.U. Medical Center, Indianapolis.

April 16: Therapeutic Advances, Reid Memorial Hospital, Richmond.

April 22: 10th Annual Arthur B. Richter Conference—"School Children: Their Trials, Tribulations and Triumphs," Adam's Mark Hotel, Indianapolis.

May 6-7: 22nd Annual Indiana Multidisciplinary Child Care Conference, Holiday Inn-Union Station, Indianapolis.

May 6-8: Radiology Update, Hyatt Regency, Indianapolis.

May 12-14: Family Practice Update Part I, Holiday Inn-Airport, Indianapolis.

May 14-15: 1987 Symposium on Ultrasound on the Breast, Holiday Inn-Airport, Indianapolis.

May 20: Alumni Day CME Program for Internists, I.U. Medical Center, Indianapolis.

For further information on these and other CME programs, contact Melody Dian, Assistant Director, CME, I.U. School of Medicine—(317) 274-8353.

Sports Medicine

The 10th Annual Sports Medicine Symposium will be conducted May 14-16 at the Sheraton Inn and Conference Center in Madison, Wisc.

Physicians, nurses, therapists, and trainers who work with athletes may attend. AMA Category 1 credit is 20 hours; AAFP credit is pending.

Contact Sarah Aslakson, 465-B WARF Bldg., 610 Walnut St., Madison, Wisc. 53705—(608) 263-2856.

Depression in the Elderly

"Depression in the Elderly: Diagnostic and Treatment Issues" is the title of a course to be given April 24-25 at the Sheraton Inn, Madison, Wisc.

The course is accredited for eight AMA Category 1 hours and eight elective AAFP hours. The cost for physicians and Ph.D.s is $175, for nurses, residents and others, $100.

The correspondent is Ann Bailey, 456 WARF Bldg., 610 Walnut St., Madison, Wisc. 53705—(608) 263-2854.

Infectious Diseases

The 31st Annual Infectious Diseases Symposium will meet May 1 at the Crown Center Hotel, Kansas City, Mo.

The symposium is accredited for Category 1 AMA and AAFP. The correspondent is Eileen Buttron, Office of CME, 39th and Rainbow Blvd., Kansas City, Kan. 66103—(913) 588-4494.

Humana Heart Institute International at Humana Hospital – Audubon is pleased to announce...

The Third International Conference Cardiovascular Disease: Problems of the 80s

April 22, 1987/The Brown Hotel
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This continuing medical education conference is designed for physicians specializing in family practice, internal medicine, cardiology, cardiovascular and thoracic surgery and other health care practitioners caring for patients with cardiovascular disease.

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Lee V. Giorgi, M.D.
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Designed to address recent advances in cardiology (invasive and non-invasive procedures, laser angioplasty, and pharmacologic therapy), this course will also provide an update on heart and heart/lung transplantation. Ethical and economic issues confronting medicine today will be discussed.

For registration information, please call or write Humana Heart Institute International, Humana Hospital – Audubon, One Audubon Plaza Drive, Louisville, Kentucky 40217. Telephone (502) 636-7135. Call toll free in Kentucky (800) 222-4332; or outside Kentucky (800) 227-3464.

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CHEMOTHERAPY ASSISTANCE PROGRAM: Provided by the Little Red Door, the CAP is a service for cancer patients who do not have insurance or other means to purchase their chemotherapy. A maximum loan of $500 is available to purchase—with vouchers—chemotherapy medications at local pharmacies. None of the funding comes from the United Way allocations; rather, donations, memorial contributions and funds allotted by the cancer society support the chemotherapy program.

To apply for CAP, call the Little Red Door at 317/925-5595. A complete intake interview, including information about insurance and financial resources, must be conducted by the patient or a family member at the Little Red Door, 1801 N. Meridian St., and only Marion County residents are eligible for this service.

HOOSIER ONCOLOGY GROUP (HOG) will meet Saturday, March 21. The meeting will be held at Winona Hospital, 3232 N. Meridian, Indianapolis. Registration begins at 8:30 a.m. and the meeting will begin at 9 a.m. For further information, contact the Hoosier Oncology Group at 317/927-2115.

AMERICAN CANCER SOCIETY SECOND NATIONAL CONFERENCE ON CANCER PREVENTION AND DETECTION will be held in Seattle, Wash. June 25-27.

The object of the conference is to increase knowledge about cancer causes, prevention, detection, and risk reduction. Presentations will have special emphasis on asymptomatic individuals, practical guidelines, future research, and community action programs.

The conference is open to primary care and public health physicians, nurses and students, as well as any other interested health care professionals. The conference is a continuing medical education program and meets the requirements for 15 hours in Category 1 for the AMA's Physician's Recognition Award.

The registration fee is $200 for physicians and dentists, and $100 for all other health professionals before June 15, 1987, and $250 and $150, respectively, thereafter. There is no charge for students, interns, residents, or American Cancer Society Fellows or Career Development Awardees.

For further information write: American Cancer Society, Second National Conference on Cancer Prevention and Detection, 90 Park Ave., New York, N.Y. 10016.

"PRE-CLINICAL STUDIES WITH TUMOR NECROSIS FACTOR" will be the presentation made by the director of the Arizona Cancer Center, Dr. Sydney E. Salmon of the University of Tucson. The lecture will take place Wednesday, April 22, in the Lilly lecture room in the Biomedical Research Building of the Eli Lilly Corporate Center. Parking is available on the corner of Merrill Street and Alabama Street in Lot 17.

This program, sponsored by the Leukemia Society and the Indiana University School of Medicine, will begin at 6 p.m. with a buffet and reception. The lecture by Dr. Salmon will begin at 8 p.m.

The lecture carries 1.5 credits of continuing medical education in Category 1. For further information contact the Leukemia Society of America, Indiana Chapter, 4720 Kingsway Dr., Indianapolis 46205, or phone 317/255-8787.

NEW PUBLICATIONS: "Advances in Cancer Control: Health Care Financing and Research," edited by Lee Mortenson, Paul Engstrom and Paul Anderson. Prevention and screening efforts, marketing issues in cancer program development and the new field of health care financing research, oncology nursing management, clinical research in community settings, and research in geographically based cancer control. To order the book contact: Alan R. Liss Inc., 41 E. 11th St., New York, N.Y. 10003, phone 212/475-7700; the price is $74.

"All About Fat and Cancer Risk," published by the American Institute for Cancer Research, explains how to cut down dietary fat. To obtain your free booklet contact the AICR, Dept. FC, Washington, D.C. 20069.

ONCOLOGY NURSING SOCIETY'S 12th Annual Congress will be held in Denver, Colorado May 6-9, 1987. The 1987 Congress sessions will provide information and continuing education in oncology nursing practice, education and research. This year's program is entitled "Reaching New Heights," and the goal is to provide a forum where participants will expand their knowledge, explore new dimensions and reaffirm their commitment to cancer care.

The registration fee is $125 for members, $190 for non-members, and $95 for students and retired nurses. For more information regarding registration contact: Oncology Nursing Society, 3111 Banksville Road, Suite 200, Pittsburgh, Pa. 15216, or call 303/892-1112.

1987 HOSPICE STUDY SEMINAR IN BRITAIN, sponsored by the Hospice Education Institute will be held in London, July 5-17, 1987. An inter-disciplinary seminar, surveying many facets of hospice care for terminally ill patients and their families; emphasizing the variety and diversity of hospice models; investigating and evaluating innovative approaches to terminal care; and stressing the importance of the professional and volunteer team. Lectures and discussions will be conducted by leading members of Britain's health and caring professions, all with a wealth of experience in hospice. For further information regarding registration, contact the Hospice Education Institute, Five Essex Square, P.O. Box 713, Essex, Connecticut 06426, or call 800-331-1620.

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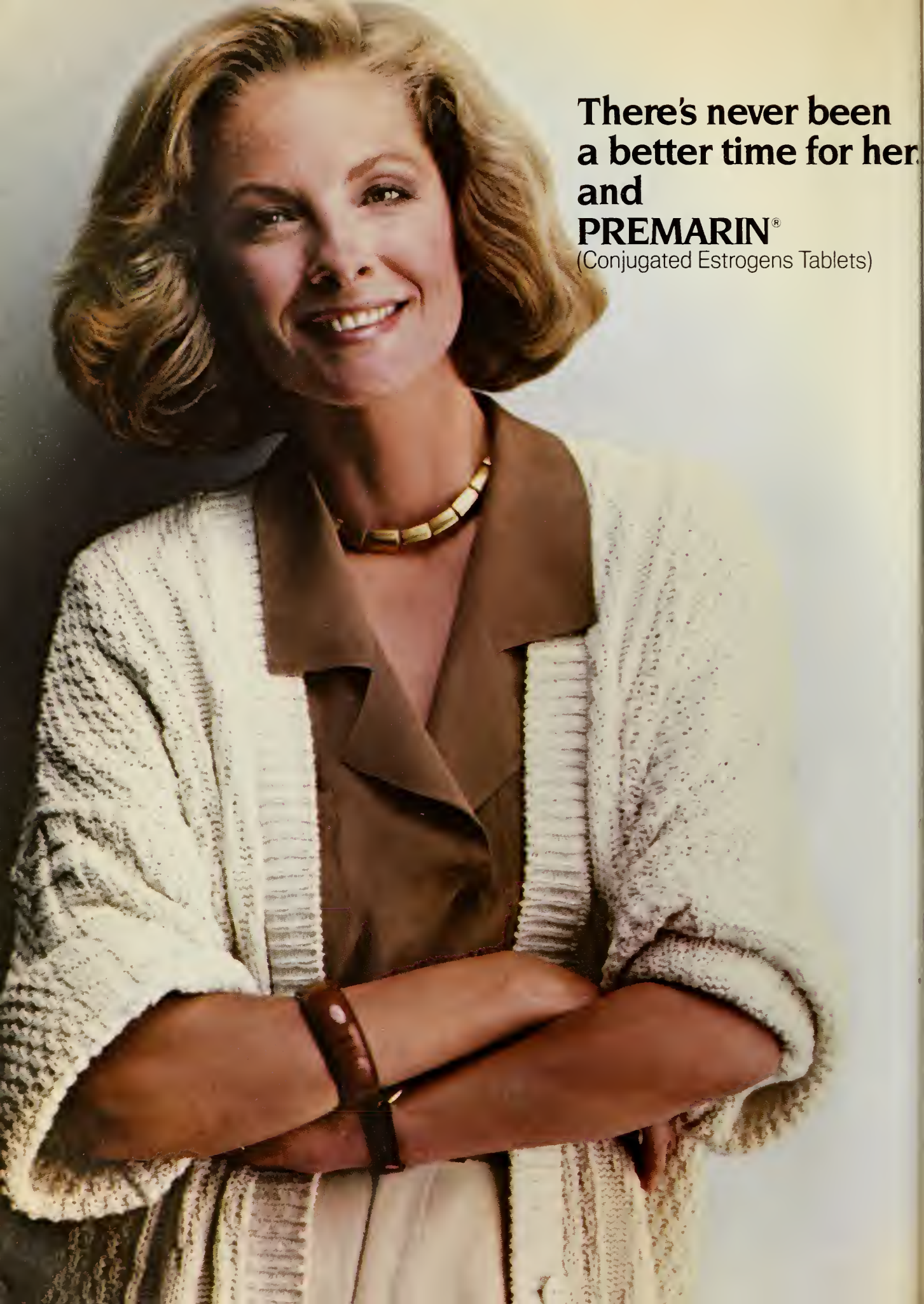


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Endometrial hyperplasia was significantly reduced when progestin was added to PREMARIN therapy for more than ten days a month.[1-4] The risk of endometrial hyperplasia may also be reduced through cyclic administration of unopposed, low-dose PREMARIN.

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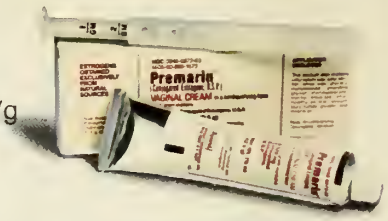
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For atrophic vaginitis

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Vaginal Cream

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BRIEF SUMMARY *(FOR FULL PRESCRIBING INFORMATION AND PATIENT INFORMATION, SEE PACKAGE CIRCULARS.)*

PREMARIN® Brand of conjugated estrogens tablets, USP
PREMARIN® Brand of conjugated estrogens Vaginal Cream in a nonliquefying base

1. ESTROGENS HAVE BEEN REPORTED TO INCREASE THE RISK OF ENDOMETRIAL CARCINOMA

Three independent case control studies have reported an increased risk of endometrial cancer in postmenopausal women exposed to exogenous estrogens for more than one year. This risk was independent of the other known risk factors for endometrial cancer. These studies are further supported by the finding that incidence rates of endometrial cancer have increased sharply since 1969 in eight different areas of the United States with population-based cancer reporting systems, an increase which may be related to the rapidly expanding use of estrogens during the last decade. The three case control studies reported that the risk of endometrial cancer in estrogen users was about 4.5 to 13.9 times greater than in nonusers. The risk appears to depend on both duration of treatment and on estrogen dose. In view of these findings, when estrogens are used for the treatment of menopausal symptoms, the lowest dose that will control symptoms should be utilized and medication should be discontinued as soon as possible. When prolonged treatment is medically indicated, the patient should be reassessed on at least a semiannual basis to determine the need for continued therapy. Although the evidence must be considered preliminary, one study suggests that cyclic administration of low doses of estrogen may carry less risk than continuous administration; it therefore appears prudent to utilize such a regimen. Close clinical surveillance of all women taking estrogens is important. In all cases of undiagnosed persistent or recurring abnormal vaginal bleeding, adequate diagnostic measures should be undertaken to rule out malignancy. There is no evidence at present that "natural" estrogens are more or less hazardous than "synthetic" estrogens at equiestrogenic doses.

2. ESTROGENS SHOULD NOT BE USED DURING PREGNANCY.

The use of female sex hormones, both estrogens and progestogens, during early pregnancy may seriously damage the offspring. It has been shown that females exposed in utero to diethylstilbestrol, a non-steroidal estrogen, have an increased risk of developing in later life a form of vaginal or cervical cancer that is ordinarily extremely rare. This risk has been estimated as not greater than 4 per 1,000 exposures. Furthermore, a high percentage of such exposed women (from 30% to 90%) have been found to have vaginal adenosis, epithelial changes of the vagina and cervix. Although these changes are histologically benign, it is not known whether they are precursors of malignancy. Although similar data are not available with the use of other estrogens, it cannot be presumed they would not induce similar changes. Several reports suggest an association between intrauterine exposure to female sex hormones and congenital anomalies, including congenital heart defects and limb reduction defects. One case control study estimated a 4.7-fold increased risk of limb reduction defects in infants exposed in utero to sex hormones (oral contraceptives, hormone withdrawal tests for pregnancy, or attempted treatment for threatened abortion). Some of these exposures were very short and involved only a few days of treatment. The data suggest that the risk of limb reduction defects in exposed fetuses is somewhat less than 1 per 1,000. In the past, female sex hormones have been used during pregnancy in an attempt to treat threatened or habitual abortion. There is considerable evidence that estrogens are ineffective for these indications, and there is no evidence from well controlled studies that progestogens are effective for these uses. If PREMARIN is used during pregnancy, or if the patient becomes pregnant while taking this drug, she should be apprised of the potential risks to the fetus, and the advisability of pregnancy continuation.

DESCRIPTION: PREMARIN (conjugated estrogens, USP) contains a mixture of estrogens, obtained exclusively from natural sources, blended to represent the average composition of material derived from pregnant mares' urine. It contains estrone, equilin, and 17α-dihydroequilin, together with smaller amounts of 17α-estradiol, equilenin, and 17α-dihydroequilenin as salts of their sulfate esters. Tablets are available in 0.3 mg, 0.625 mg, 0.9 mg, 1.25 mg, and 2.5 mg strengths of conjugated estrogens. Cream is available as 0.625 mg conjugated estrogens per gram.

INDICATIONS AND USAGE: PREMARIN (conjugated estrogens tablets, USP): Moderate-to-severe *vasomotor* symptoms associated with the menopause. (There is no evidence that estrogens are effective for nervous symptoms or depression without associated vasomotor symptoms and they should not be used to treat such conditions.) **Osteoporosis (abnormally low bone mass).** Atrophic vaginitis. Kraurosis vulvae. Female castration.

PREMARIN (conjugated estrogens) Vaginal Cream is indicated in the treatment of atrophic vaginitis and kraurosis vulvae. PREMARIN HAS NOT BEEN SHOWN TO BE EFFECTIVE FOR ANY PURPOSE DURING PREGNANCY AND ITS USE MAY CAUSE SEVERE HARM TO THE FETUS (SEE BOXED WARNING).

Concomitant Progestin Use: The lowest effective dose appropriate for the specific indication should be utilized. Studies of the addition of a progestin for 7 or more days of a cycle of estrogen administration have reported a lowered incidence of endometrial hyperplasia. Morphological and biochemical studies of the endometrium suggest that 10 to 13 days of progestin are needed to provide maximal maturation of the endometrium and to eliminate any hyperplastic changes. Whether this will provide protection from endometrial carcinoma has not been clearly established. There are possible additional risks which may be associated with the inclusion of progestin in estrogen replacement regimens. (See PRECAUTIONS.) The choice of progestin and dosage may be important; product labeling should be reviewed to minimize possible adverse effects.

CONTRAINDICATIONS: Estrogens should not be used in women (or men) with any of the following conditions: 1. Known or suspected cancer of the breast except in appropriately selected patients being treated for metastatic disease. 2. Known or suspected estrogen-dependent neoplasia. 3. Known or suspected pregnancy. (See Boxed Warning). 4. Undiagnosed abnormal genital bleeding. 5. Active thrombophlebitis or thromboembolic disorders. 6. A past history of thrombophlebitis, thrombosis, or thromboembolic disorders associated with previous estrogen use (except when used in treatment of breast or prostatic malignancy).

WARNINGS: Long-term continuous administration of natural and synthetic estrogens in certain animal species increases the frequency of carcinomas of the breast, cervix, vagina, and liver. There are now reports that estrogens increase the risk of carcinoma of the endometrium in humans. (See Boxed Warning.) At the present time there is no satisfactory evidence that estrogens given to postmenopausal women increase the risk of cancer of the breast, although a recent study has raised this possibility. There is a need for caution in prescribing estrogens for women with a strong family history of breast cancer or who have breast nodules, fibrocystic disease, or abnormal mammograms. A recent study has reported a 2- to 3-fold increase in the risk of surgically confirmed gallbladder disease in women receiving postmenopausal estrogens.

Adverse effects of oral contraceptives may be expected at the larger doses of estrogen used to treat prostatic or breast cancer or postpartum breast engorgement; it has been shown that there is an increased risk of thrombosis in men receiving estrogens for prostatic cancer and women for postpartum breast engorgement. Users of oral contraceptives have an increased risk of diseases, such as thrombophlebitis, pulmonary embolism, stroke, and myocardial infarction. Cases of retinal thrombosis, mesenteric thrombosis, and optic neuritis have been reported in oral contraceptive users. An increased risk of postsurgery thromboembolic complications has also been reported in users of oral contraceptives. If feasible, estrogen should be discontinued at least 4 weeks before surgery of the type associated with an increased risk of thromboembolism, or during periods of prolonged immobilization. Estrogens should not be used in persons with active thrombophlebitis, thromboembolic disorders, or in persons with a history of such disorders in association with estrogen use. They should be used with caution in patients with cerebral vascular or coronary artery disease. Large doses (5 mg conjugated estrogens per day), comparable to those used to treat cancer of the prostate and breast, have been shown to increase the risk of nonfatal myocardial infarction, pulmonary embolism and thrombophlebitis. When doses of this size are used, any of the thromboembolic and thrombotic adverse effects should be considered a clear risk.

Benign hepatic adenomas should be considered in estrogen users having abdominal pain and tenderness, abdominal mass, or hypovolemic shock. Hepatocellular carcinoma has been reported in women taking estrogen-containing oral contraceptives. Increased blood pressure may occur with use of estrogens in the menopause and blood pressure should be monitored with estrogen use. A worsening of glucose tolerance has been observed in patients on estrogen-containing oral contraceptives. For this reason, diabetic patients should be carefully observed. Estrogens may lead to severe hypercalcemia in patients with breast cancer and bone metastases.

PRECAUTIONS: Physical examination and a complete medical and family history should be taken prior to the initiation of any estrogen therapy with special reference to blood pressure, breasts, abdomen, and pelvic organs, and should include a Papanicolaou smear. As a general rule, estrogen should not be prescribed for longer than one year without another physical examination being performed. Conditions influenced by fluid retention such as asthma, epilepsy, migraine, and cardiac or renal dysfunction, require careful observation. Certain patients may develop manifestations of excessive estrogenic stimulation, such as abnormal or excessive uterine bleeding, mastodynia, etc. Prolonged administration of unopposed estrogen therapy has been reported to increase the risk of endometrial hyperplasia in some patients. Oral contraceptives appear to be associated with an increased incidence of mental depression. Patients with a history of depression should be carefully observed. Preexisting uterine leiomyomata may increase in size during estrogen use. The pathologist should be advised of estrogen therapy when relevant specimens are submitted. If jaundice develops in any patient receiving estrogen, the medication should be discontinued while the cause is investigated. Estrogens should be used with care in patients with impaired liver function, renal insufficiency, metabolic bone diseases associated with hypercalcemia, or in young patients in whom bone growth is not complete. If concomitant progestin therapy is used, potential risks may include adverse effects on carbohydrate and lipid metabolism.

The following changes may be expected with larger doses of estrogen:

a. Increased sulfobromophthalein retention.

b. Increased prothrombin and factors VII, VIII, IX, and X; decreased antithrombin 3; increased norepinephrine-induced platelet aggregability.

c. Increased thyroid binding globulin (TBG) leading to increased circulating total thyroid hormone, as measured by PBI, T4 by column, or T4 by radioimmunoassay. Free T3 resin uptake is decreased, reflecting the elevated TBG; free T4 concentration is unaltered.

d. Impaired glucose tolerance.

e. Decreased pregnanediol excretion.

f. Reduced response to metyrapone test.

g. Reduced serum folate concentration.

h. Increased serum triglyceride and phospholipid concentration. As a general principle, the administration of any drug to nursing mothers should be done only when clearly necessary since many drugs are excreted in human milk.

ADVERSE REACTIONS: The following have been reported with estrogenic therapy, including oral contraceptives: breakthrough bleeding; spotting; change in menstrual flow; dysmenorrhea; premenstrual-like syndrome; amenorrhea during and after treatment; increase in size of uterine fibromyomata; vaginal candidiasis; change in cervical erosion and in degree of cervical secretion; cystitis-like syndrome; tenderness, enlargement, secretion (of breasts); nausea, vomiting; abdominal cramps; bloating; cholestatic jaundice; chloasma or melasma which may persist when drug is discontinued; erythema multiforme; erythema nodosum; hemorrhagic eruption; loss of scalp hair; hirsutism; steepening of corneal curvature; intolerance to contact lenses; headache, migraine; dizziness; mental depression; chorea; increase or decrease in weight; reduced carbohydrate tolerance; aggravation of porphyria; edema; changes in libido.

ACUTE OVERDOSAGE: May cause nausea, and withdrawal bleeding may occur in females.

DOSAGE AND ADMINISTRATION:

PREMARIN® Brand of conjugated estrogens tablets, USP

1. *Given cyclically for short-term use only.* For treatment of moderate to severe *vasomotor* symptoms, atrophic vaginitis, or kraurosis vulvae associated with the menopause (0.3 to 1.25 mg or more daily). The lowest dose that will control symptoms should be chosen and medication should be discontinued as promptly as possible. Administration should be cyclic (eg, three weeks on and one week off). Attempts to discontinue or taper medication should be made at three- to six-month intervals.

2. *Given cyclically.* Female castration. Osteoporosis. Female castration—1.25 mg daily, cyclically. Adjust upward or downward according to response of the patient. For maintenance, adjust dosage to lowest level that will provide effective control. Osteoporosis —0.625 mg daily. Administration should be cyclic (eg, three weeks on and one week off).

Patients with an intact uterus should be monitored for signs of endometrial cancer and appropriate measures taken to rule out malignancy in the event of persistent or recurring abnormal vaginal bleeding.

PREMARIN® Brand of conjugated estrogens Vaginal Cream

Given cyclically for short-term use only. For treatment of atrophic vaginitis or kraurosis vulvae.

The lowest dose that will control symptoms should be chosen and medication should be discontinued as promptly as possible.

Administration should be cyclic (eg, three weeks on and one week off).

Attempts to discontinue or taper medication should be made at three-to-six month intervals.

Usual dosage range: 2 to 4 g daily, intravaginally, depending on the severity of the condition.

Treated patients with an intact uterus should be monitored closely for signs of endometrial cancer and appropriate diagnostic measures should be taken to rule out malignancy in the event of persistent or recurring abnormal vaginal bleeding.

References:

1. Whitehead MI, Townsend PT, Pryse-Davies J, et al: Effects of estrogens and progestins on the biochemistry and morphology of the postmenopausal endometrium. *N Engl J Med* 1981;305:1599-1605. **2.** Paterson MEL, Wade-Evans T, Sturdee DW, et al: Endometrial disease after treatment with oestrogens and progestogens in the climacteric. *Br Med J* 1980;280:822-824. **3.** Magos AL, Brincat M, Studd JWW, et al: Amenorrhea and endometrial atrophy with continuous oral estrogen and progestogen therapy in postmenopausal women. *Obstet Gynecol* 1985;67:496-499. **4.** Whitehead MI, Lane G, Siddle N, et al: Avoidance of endometrial hyperstimulation in estrogen-treated postmenopausal women. *Semin Reprod Endocrinol* 1983;1:1;41-52. **5.** Barnes RB, Roy S, Lobo RA: Comparison of lipid and androgen levels after conjugated estrogen or depo-medroxyprogesterone acetate treatment in postmenopausal women. *Obstet Gynecol* 1985;66:216-219.

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To obtain Category 1 credit for this month's article, complete the quiz on page 285.



Treatment of Myasthenia Gravis

RAHMAN POURMAND, M.D.
Indianapolis

PART 1

NOTE: For ease of comprehension, this article is being presented in two parts. Appropriate references are provided at the end of each part. The CME quiz (page 285) encompasses both parts.

The author will discuss Myasthenia Gravis in a live presentation on the I.U. School of Medicine's Medical Television Network from noon to 1 p.m. on Monday, March 23.

For information concerning CME accreditation for MTN programs, call the CME office at (317) 274-8353.

General Consideration

Despite numerous modalities of treatment in Myasthenia Gravis (MG), there is no unique formula for treatment, and it must be individualized and tailored for each patient. This lack of uniformity arises since the natural history of the disease is unknown and controlled clinical trials in the treatment of this disorder are few.[1] However, in lieu of this, a number of observations have provided evidence for specific immunologic abnormalities in this condition. Therefore, the treatment would logically be directed toward the correction of these abnormalities. In the first part of this discussion, the current treatment for acquired autoimmune generalized MG will be discussed and in Part 2 the discussion will cover other forms of MG, plasma exchange, other immunosuppressive therapy and, finally, the diagnosis and management of crisis in MG.

Pharmacotherapy:
Anticholinestrase (AchE) Drugs

These agents have been, and still are, the first-line drugs for the management of MG.[2] These drugs inhibit the destruction and/or hydrolysis of acetyocholine which makes it more

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available at the receptor site, therefore, enhancing and prolonging the neuromuscular transmission.[3] Generally, they have been used in any type of adult MG (*Table 1*). They are particularly valuable in ocular myasthenia and/or mild generalized MG.

However, in recent years, since the introduction of corticosteroids and other immunosuppressant drugs, the role of AchE has declined and is now used primarily for symptomatic relief. The symptomatic improvement, however, has a great effect in the life quality of many patients. Pyridostigmine bromide (Mestinon), neostigmine bromide (Prostigmine), and ambenomium chloride (Mytelase) are the most common AchEs.

Mestinon is preferred because it has the least side effects, is steady acting, and is available in various forms (tablets, syrup and parenteral). The 60mg tablet is equal to 5cc of syrup or 2mg intramuscular injection. Mestinon also comes in 180mg timespan for nighttime use. In the adult, the initial dose is usually 60mg q 4-6 hrs. Adjustment of the dosage would be based upon trial and error, on clinical response and/or upon response to the intravenous edrophonium chloride (Tensilon) test given at the peak or through the decline phase (e.g., 2-3 hours after the last dose).

The dose of Mestinon is variable from patient to patient, and even in single individuals, from day to day, and also when other underlying conditions such as infection, menstrual period, surgery, etc. exist. It also has been shown that different muscles respond differently (some get better, some worse). In this situation, it is wise to adjust the dose according to the response of the muscles, which is of the most concern at the time (e.g., respiratory, bulbar).

To overcome undesirable muscarinic side effects, which usually include extreme salivation, lacrimation, increase in bronchial secretions, abdominal cramps and bradycardia, many clinicians use atropine. However, if at all possible, its use should be avoided, because the signs of overdose can easily be missed by the patient and the physician. Therefore, during the introductory phase of AchE therapy, if muscarinic symptoms are significant, but the patient's weakness is responding to the Mestinon, atropine may be used with caution.

Most patients respond to AchE, but, unfortunately, these agents usually produce less than optimal relief and are less effective with chronic use, and some patients would not respond at all. Therefore, it appears that AchEs are not dependable agents, particularly in the case of generalized and/or severe forms of MG. In these cases, other modalities of treatment should be adopted sooner or later in the course of the disease. In mild cases of generalized and/or purely ocular forms of MG, one may use AchE agents as the sole therapy, until the clinical status changes (e.g., ocular changes to generalized). At any rate, in generalized MG, after optimal response to AchE is achieved, the next step would be a thymectomy, regardless of the prior use of corticosteroids.

TABLE 1
Clinical Classification (Modified Osserman) of MG

Class	Distribution
I	Ocular
II	Mild generalized weakness, usually with ocular muscle weakness
III	Predominantly bulbar involvement, usually with mild generalized weakness
IV	Moderate generalized weakness
V	Severe generalized weakness

Corticosteroids

The rationale for using corticosteroids in patients with MG is based upon alteration of the immune system in this disease, which is now well established as being an autoimmune disorder.[6-10] Among the corticosteroids, Prednisone is the most frequently used. Generally, 80-90% of the patients respond favorably to Prednisone.[11-15] From these reviews, the indications for corticosteroids are:

1) All patients with generalized MG, who are not responding favorably to AchE.
2) In ocular MG, if the symptoms are disabling according to the patients' life quality, or they are not responding adequately to AchE.
3) Patients with thymoma, whether they have ocular or generalized MG, before and after removal of the thymus gland.
4) Failure to respond adequately to thymectomy, which could be acute exacerbation following surgery and/or delayed improvement.
5) Late onset of MG, particularly in males.[12]

Before initiation of corticosteroids, the benefits and risks should be discussed with the patients and relatives and the long-term side effects should be discussed.

The rationale behind using steroids in this disease are:

1) Strong evidence of immunological abnormalities in pathogenesis.
2) Marked improvement and/or remission in up to 80% of patients (*Table 2*).
3) Improvement in a predictable time response.
4) Reduction of morbidity and mortality in thymectomy.
5) Availability in various forms.

Once the patient is selected for Prednisone therapy, hospitalization is mandatory. The reason for this is that approximately half of the patients may show temporary worsening, particular-

TABLE 2
Definition of Responses to Prednisone Treatment

Response	Definition
Remission	Normal function and manual muscle examination (may have weakness of eye closure only). Receiving no cholinesterase inhibitors.
Marked Improvement	Normal function, may receive cholinestrase inhibitors. Weakness on manual muscle testing.
Improvement	Significantly greater strength on manual muscle testing than prior to treatment.
Failed	No consistent improvement over pretreatment function or strength.

ly those treated with a high dose of Prednisone. This exacerbation may occur from the first day to about one month after starting the Prednisone. On the average, it occurs between 6-10 days after Prednisone is started.

For the initiation of Prednisone, the selection of the dosage may be made from:

1) Low dose with gradual increment.
2) High dose daily.
3) Alternating high dose.

A high daily dose regimen, however, produces a faster and more complete improvement. If the latter is selected for adults, the initial dose is usually about 60mg per day. When the patient shows sustained improvement (usually in two to three weeks), the dose may be given on alternate days (usually twice the daily dose). Thereafter, the dose will be tapered gradually until the smallest necessary dose is achieved. The patient may remain on this small dose for an indefinite period. Similarly, the AchE medications may be tapered off according to the patient's requirement. When the patient shows a steady and moderate to marked improvement on a high alternate dose (60-80mg), a thymectomy may then be considered. On the average, it takes about 2-6 months before performing the thymectomy.

The major drawback in steroid therapy is its side effects which commonly develop since steroids are used chronically in this condition to achieve sustained improvement. However, most of these side effects are reversible by reducing the dose. Another problem with Prednisone therapy is the recurrence of weakness upon the reduction of the dose, particularly if it is reduced too quickly. It is recommended that the dose reduction rate be 5-10mg per month.

Thymectomy

Although the role of the thymus gland in the pathogenesis of MG is still a mystery, the value of thymectomy has been reported by numerous studies.[6-27] However, these studies are not controlled and/or prospective. According to retrospective literature, this procedure will provide improvement in 60-80% of patients to some extent at some point in their illness. The onset of the improvement in the symptoms of MG following this procedure is unclear. However, it should be kept in mind that the thymectomy is an elective surgery. The patient should be informed of its benefits and also of the risks.

In most centers now, this procedure is recommended to all patients with generalized MG, from mild to moderately severe, if they have no medical contraindications to the surgery. In purely ocular MG, which has been confirmed by electrophysiological and immunological factors, the role of thymectomy is more controversial although a beneficial effect has been reported.[28] Therefore, it can be stated that in all patients with generalized MG with and/or without thymoma, and without respect to age or sex, at some point in the illness, a thymectomy is to be considered.

According to the literature, early thymectomy is better and more effective.[18] As mentioned previously, the patient should be stabilized from a myasthenic standpoint, and be in a stage of moderate to marked improvement prior to the thymectomy. This stabilization can be obtained by anticholinestrase, Prednisone, and/or plasma exchange.[26] The most practical and reliable way of achieving this is corticosteroid therapy. However, whether or not to immunosuppress the patient before the thymectomy is an unresolved issue.[4,5] The rationale for such (immunosuppressive) therapy is:

1) Stabilizing the patient's condition by strengthening vital musculature.
2) Decreasing morbidity and mortality of the procedure.
3) More sustained improvement.

The response of patients to thymectomy is variable. This response may be achieved for as long as five to six years. Most studies show an average steady response after thymectomy at 2 1/2 years. Therefore, it appears that there is no clear indication that this procedure should be performed on an emergency basis without stabilization of the patient's condition prior to surgery. In some instances, however, this procedure would need to be performed as early as possible, such as in patients with invasive thymoma. In circumstances in which a thymectomy needs to be obtained urgently, a plasma exchange or a short course of corticosteroids would be logical.[26,29]

The reasons for doing a thymectomy on all patients with generalized MG are:

1) An increase in the chance for remission.

2) Better control of the disease.
3) Decrease in the chance for relapse after stopping immunosuppressive drugs.
4) Increase in the long-term survival rate.

The choice of the surgical approach to the thymectomy is a matter of debate. Generally, this procedure is performed either by cervical approach or sternal splitting incision. The selection, however, is primarily dependent on the surgeon's experience and his or her morbidity/mortality rate in that particular center. However, most major centers prefer to do transternal surgery because of its lower rate of morbidity and mortality and, because it permits the total removal of the thymus gland. The important point that needs to be addressed here is that, if the patient elects to be thymectomized, it is recommended that the patient be sent to a center that has the facilities and the experience with such procedures and patient population.

Preparation of Patients for Thymectomy

Patients who have elected to have a thymectomy should be at the best possible functional level regarding strength (muscle), particularly the vital muscles such as bulbar and respiratory. Prior to surgery, besides the routine check-up of the patient, vital capacity and pulmonary function tests, and arterial blood gases testing are critical. If the patient is taking cholinesterase inhibitors, they should be decreased and/or discontinued if possible. Immunosuppressive drugs, including Prednisone, may be continued. If required, anticholinesterase can be given parenterally for decreasing the secretions of the upper respiratory tract. If necessary, atropine may be added. If the patient is taking Prednisone for prevention of adrenal insufficiency during surgery, the patient should be given parenteral hydrocortisone. Several ways have been recommended for giving parenteral corticosteroids before, during and after surgery. These are:

1) Administration of an equal and slightly above the maintainence dose of Prednisone with hydrocortisone on a daily basis.

2) 100mg intramuscular hydrocortisone just before surgery and continuing 100mg hydrocortisone in each liter of intravenous infusion just before, during and two days after surgery; the total amount of hydrocortisone, in this way, would be about 300-500mg.[30]

3) One gram of hydrocortisone in 400cc of 5% dextrose and water started one hour before surgery. During that hour, 100cc solution is given that is approximately 200mg hydrocortisone; and 100cc is administered during the first hour of surgery, and another 100cc given during the second hour. This solution is given at the rate of 20cc per hour.[29]

Of all these methods, the simplest way is to administer parenteral hydrocortisone equal to the oral maintainance dose of Prednisone.

For sedation, a minor dose of tranquilizers, such as barbituate and/or Demerol, can be given. For the induction of anesthesia, pentobarbital can be used; however, a combination of Halothane and nitrous oxide is the safest selection. For relaxation of the muscles during surgery, succinylcholine may be used, but it is better to start with a low dose and to increase it if necessary. If the surgeon prefers to use prophylactic antibiotics, cephalosporines are the best choice. It is also important to inform patients that after surgery they may become weak, but that this is likely to be transient and can be managed by supportive measures.

Postoperative Care

After surgery, the patient usually is transferred to the recovery room. However, it is very important that these patients be transferred immediately to the Intensive Care Unit and stay for at least 36-48 hours. This is important in view of the nursing care, for it requires close monitoring of the vital functions, frequent suction of the trachea and upper respiratory apparatus, chest percussion, pulmonary physical therapy, along with monitoring vital capacity very closely. For relief of pain after surgery, which is common, particularly after mediastinal splitting, Demerol is most satisfactory. Morphine can be used at a lower dose.

It is not necessary to rush to reinstitute anticholinesterase after the patient wakes up from surgery. These patients are being taken care of in the Intensive Care Unit, are under close observation and are in a resting state. Therefore, the recommendation is not to start anticholinesterase medication for at least 12-24 hours after surgery. After that period, the patient may be started on a low dose of anticholinesterase such as Mestinon, 60mg over three to four hours, and adjusted according to the clinical response or the Tensilon® (edrophonium) Test.

If the patient shows postoperative worsening, plasma exchange should be considered, if available. However, if the worsening is not critical, one may wish to begin corticosteroids in the form of Prednisone or ACTH, if the patient has not been on these drugs before the surgery. The duration of hospitalization in uncomplicated thymectomies is usually four to five days. After discharge, the patient should be followed more closely for three to six months. The maintenance medications should be continued for at least one month before the decision to taper off.

Conclusion

Current recommendations for management of patients with MG (acquired, adult type) with and/or without thymoma can be summarized as:

1) Completion of firm diagnosis of MG and exclusion of other possibilities that could mimic this condition.

2) Education of patients and relatives about the disease and management.

3) The wearing of a medical alert bracelet or necklace is highly recommended.

4) Pharmacotherapy of this condi-

tion commonly begins with AchE for all forms of MG. For purely ocular MG, one may wish to use AchE as the sole drug.

5) If a patient has generalized MG, with and/or without thymoma, immunosuppressive treatment, prior to thymectomy, is thought to decrease the morbidity and mortality of this procedure. It has been recommended that these patients be treated with Prednisone on an alternate daily dose until they reach a steady marked or moderate improvement. After this improvement is achieved, the thymectomy will be performed.

6) If the patient needs to be thymectomized sooner (e.g., invasive thymoma) plasma exchange and/or a short course of corticosteroid therapy prior to surgery would be beneficial.

7) Although it is almost impossible to draw a unique formula for treating these patients,[1] it appears that the final goal is doing a thymectomy after they have been adequately stabilized.

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PART 2

In Part 1 of this article, the usual treatment of myasthenia gravis (MG) was described. However, a limited number of patients with MG do not respond adequately. Fortunately, the percentage of non-responders is low. Who will respond to treatment and who will not is unpredictable; the factors determining the outcome are unknown. For these patients, however, there are several modalities of treatment which will be described briefly.

As mentioned, patients who do not respond adequately to anticholinestrase (AchE) drugs usually respond to Prednisone treatment in 80-85% of the cases. However, there is still a low percentage of patients who do not even respond to Prednisone adequately, or who become resistant to it or develop serious side effects. When an early thymectomy is planned and the patient does not respond to Prednisone ade-

quately after the thymectomy, a plasma exchange is an option to be considered. However, in a patient who is nonresponsive to Prednisone, if a thymectomy can be delayed, the best choice would be adding immunosuppressive drugs.

Immunosuppressive Drugs

The role of immunosuppressive drugs in the treatment of MG is mainly recognized in European countries, which began using these drugs in the past two decades. The American literature in this regard is rather scanty. These drugs include 6-mercaptuopurine, cyclophosphamide and azathioprine.

The recent studies are primarily focused on the use of the azathioprine (Aza) in the treatment of MG. The literature suggests that Aza is effective and that patients achieve improvement in 80-90% of the cases.[1-8] The remission rate reported in recent studies is 40-45%. However, from these studies it is difficult to quantitate the amount of improvement and, furthermore, the studies are uncontrolled and it is difficult to assess whether Aza alone works better or with a combination of Prednisone therapy and/or thymectomy. Also, the patients in these studies have been treated with multiple immunosuppressive drugs and have had a thymectomy or even plasma exchange prior to the use of Aza.

In some European centers (6), patients with generalized MG are routinely treated with Prednisone and Aza after the diagnosis has been established. After this initial period, the Prednisone is tapered off and Aza is then continued. It appears that in European countries this drug is now recommended as the first line of treatment of generalized MG, particularly if clinically severe.

In the United States, Aza is still considered to be a second or third line drug and is used for patients who do not respond adequately to conventional therapy, such as AchE, Prednisone, and/or thymectomy. Until the results of controlled studies in a large series appear in the literature, the immunosuppressive drugs are recommended for:

1) Those patients who do not respond adequately, or who are refractory to conventional Prednisone therapy and/or thymectomy.

2) Patients who have unsustained and fluctuating symptoms of the MG while tapering off the Prednisone.

3) Patients who have had plasma exchange or thymectomy.

4) Patients who need to be immunosuppressed for a longer time, but develop undesirable serious side effects to corticosteroids.

5) Those patients who have severe generalized MG requiring immunosuppressive therapy, but use of corticosteroids are contraindicated.

6) Patients with mild MG which is not life-threatening and do not require aggressive and/or fast immunosuppressive treatment (e.g., Bulbar type in elderly).

A disadvantage of Aza is that the effect usually takes several months (2-14 months) with an average being around 12 months. Therefore, it appears that this medication is not the first drug of choice regarding immunosuppressive treatment in patients who have moderate to severe generalized MG. The other disadvantage is that we do not know the long-term side effects of this drug. The commonly known side effects are leukopenia and elevation of liver enzymes, which are usually reversible by tapering off the dose or discontinuing the drug.[9] The risk of acquired malignancy is still unknown.

One serious side effect of this medication, which could be fatal, is the risk of infection. The recommended dose for initiation of Aza is approximately 2-2.5mg per kg of body weight. The recommendation is to start the adult patient with a dose of 50mg per day and gradually increment it. The CBC and liver function should be monitored closely during the first few months, and in each follow-up visit thereafter. These drugs should not be used by women of childbearing age; if, in fact, it is given to such individuals, contraceptive measures should be considered.

Other modalities of immunosuppressive treatment, such as immunoglobulin injections, total body radiation, pre-operative thymus and mediastinal irradiation and thoracic duct drainage, have not been studied extensively; therefore, their role in the treatment of MG is as yet unclear.

Plasma Exchange (Plasmapherisis)

The rationale for doing plasma exchange (PEx) in patients with MG is to remove anti-nicotinic receptor antibody, which has been well elevated in the majority of patients with acquired generalized MG. After Pinching reported[10] improvement in a small group of patients, PEx was tried in a large patient population by other investigators.[10-13] General indications for plasma exchange are:

a) Patients who are refractory to conventional treatment (Prednisone, anticholinestrase and/or immunosuppressive drugs).

b) Myasthenic crisis (cholinergic or myasthenic).

c) Preparation for thymectomy and/or post-thymectomy worsening.

d) Acute worsening during tapering off of corticosteroids and/or other immunosuppressive drugs.

e) Unacceptable drug side effects (steroids), or contraindication to using corticosteroids, or immunosuppressive drugs.

The frequency of exchange depends upon the clinical status of the patients and the clinician's judgment. The replacement for exchange plasma could be albumin and saline with or without potassium, plasma protein with or without potassium and calcium, and Ringer's lactate and dextrane. Heparin and citrate dextrose can be employed as anticoagulants. Almost all patients with acquired MG will improve at least temporarily after plasma exchange. This improvement usually begins after the second or third exchange. The

onset, degree and duration of this improvement is mainly related to the frequency and amount of plasma exchanged.

Improvement, however, usually lasts for only a few weeks or months and gradually loses its effectiveness unless a thymectomy is performed and/or another immunosuppressive drug is added. Removal of large volumes of plasma over a short period of time may cause hypotension, bradycardia and dehydration, particularly in elderly people. These symptoms, however, can be relieved by administration of fluids and protein solutions. Patients who receive ACD (acid citrate dextrose) as anticoagulants may experience paresthesia around the mouth during the exchange; this can be alleviated by reduction of the infusion rate or intravenous administration of calcium. The serious complications of this procedure, however, are thrombophlebitis and/or bacterial endocarditis.

Treatment of Other Forms of Myasthenia Gravis

Neonatal Myasthenia: This kind of MG usually occurs in 10-20% of infants born to mothers who have MG. The symptoms usually occur about one day after birth. These newborns are at high risk for developing MG within the first week after birth and should be observed very closely for the first four to five days. The absence of neonatal MG in previous babies does not guarantee the absence of MG in subsequent newborns. Furthermore, the severity in newborn myasthenia does not correlate with the level of antibody against AchE receptor in the mother's serum.

The clinical presentation usually includes feeding difficulties, weakness, hypotonia, depressed reflexes, respiratory difficulties and, sometimes, ptosis and ophthalmaplegia. The diagnosis can be confirmed by using intramuscular neostigmin. If the child requires treatment, 4-10mg of Mestinon or 1-2mg neostigmine can be given by mouth or via a nasal gastric tube. Atropine may be needed to control muscarinic side effects. If there is difficulty in feeding due to bulbar weakness, medication may be given 30 minutes before feeding. Early plasma exchange may be considered in these newborns, if feeding difficulties are present. If fetal movements during the pregnancy are significantly diminished, which is extremely rare in this condition, plasmapheresis of the mother may be suggested.[14] The mortality of this type of myasthenia, if properly treated, is extremely low.

Congenital Myasthenia: This form of myasthenia gravis is usually carried by mothers who do not have MG, and the clinical condition is relatively persistent throughout the patient's life.[15] There are generally two forms of this type of MG. One, mainly involving the ocular muscle, presents with total ophthalmaplegia with minor involvement of the limbs and facial muscles. The other type involves mainly the bulbar and extremity muscles, with mild involvement of the ocular muscles. Antibodies to acetycholine receptor have not been demonstrated in these patients. Therefore, immunosuppressive drugs and thymectomy do not have any role in the treatment. Most patients will have a normal life expectancy with AchE medications, despite remaining at least partially disabled.

Juvenile Myasthenia: This type of MG usually begins at about age 10 years.[15] The treatment is usually similar to the adult type, although the response to AchE medications and immunosuppressive drugs is not as dramatic in adult types. Therefore, it is recommended that early thymectomy in these patients be performed.

Drug Induced Myasthenia Gravis: Several medications, including aminoglycoside antibiotics, anticonvulsants, and anti-cardiac arrhythmic drugs, are known to produce myasthenic features. The treatment is simply to withdraw the drugs. However, there is a special entity in which MG follows the use of penicillamine, particularly in patients with rheumatoid arthritis.[16,17] Although the majority of these patients will respond to the discontinuation of this agent, a certain percentage of patients require further treatment, such as AchE drugs and/or corticosteroids. If they develop respiratory insufficiency, they may even need plasma exchange. If after one year of following the discontinuation of penicillamine, the patient still has myasthenic symptoms, the patient should be treated as an adult with acquired MG as previously described.

Myasthenia Gravis in Pregnancy

Although MG can exacerbate during pregnancy, a small percentage of these patients may go to, at least, transient remission. However, the majority of these patients show no significant changes in their clinical status during pregnancy. The treatment of the myasthenic mother is similar to acquired adult type MG. In most of these patients, it is better that the MG be optimally prior to a planned pregnancy. This can be achieved by doing thymectomy and, if necessary, corticosteroid and/or plasma exchanges.

If, during the pregnancy, toxemia develops, magnesium sulfate should not be given because of the curare-like effect of this drug. If an obstetrical procedure, such as a C-section, is to be done during this time, an epidural anesthesia is preferred. If a general anesthesia is required, precautionary measures as described during thymectomy should be instituted. It is wise not to perform a thymectomy during pregnancy. Furthermore, as mentioned previously, the mother should not only be observed for exacerbation of the MG, but the fetus should be closely monitored throughout the pregnancy by a team consisting of an obstetrician and neurologist.

Crisis: Crisis in MG is defined as a rapid weakening of respiratory and generalized musculature of the body that requires intensive treatment and artificial support. This may be due to relative excessive AchE medications (cholinergic) and/or relative insufficiency of these drugs (myasthenic). The

mortality rate in crisis is about 5%, a significant reduction over the past two decades. It is important to prevent the occurrence of the crisis and recognize the signs of impending crisis. Therefore, it should be kept in mind that even myasthenic patients who are in a stage of marked improvement should be considered to be potentially ill, because at any time they may go into crisis. Recognition of impending crisis is difficult because of non-specific symptoms such as tachycardia, restlessness, difficulty in sleeping, dyspnea, and generalized malaise that may rapidly change to more objective generalized, respiratory and bulbar muscle weakness. Therefore, patients suspected of having some decompensation in the MG, should be watched very closely, and even hospitalized.

Do not try to adjust the medication via a telephone conversation. In an impending crisis, the presence of tachycardia and dyspnea may require intubation before changes of vital capacity and blood gases. In the occurrence of crisis, one should not spend excessive time in the differentiation between cholinergic and myasthenic crisis. The main goal is to keep the patient alive and then to look for the cause.

Therefore, patients presenting in crisis should be admitted to the Intensive Care Unit, their respiratory and bulbar functions should be assessed immediately, and vital signs should be stabilized. If necessary, the patient should be intubated and the airway secured. Then proceed to identify the cause and precipitating factors. Underlying infection is a very common cause. Most patients who have repeated crisis generally have significant bulbar and muscle weakness that can easily produce aspiration pneumonia.

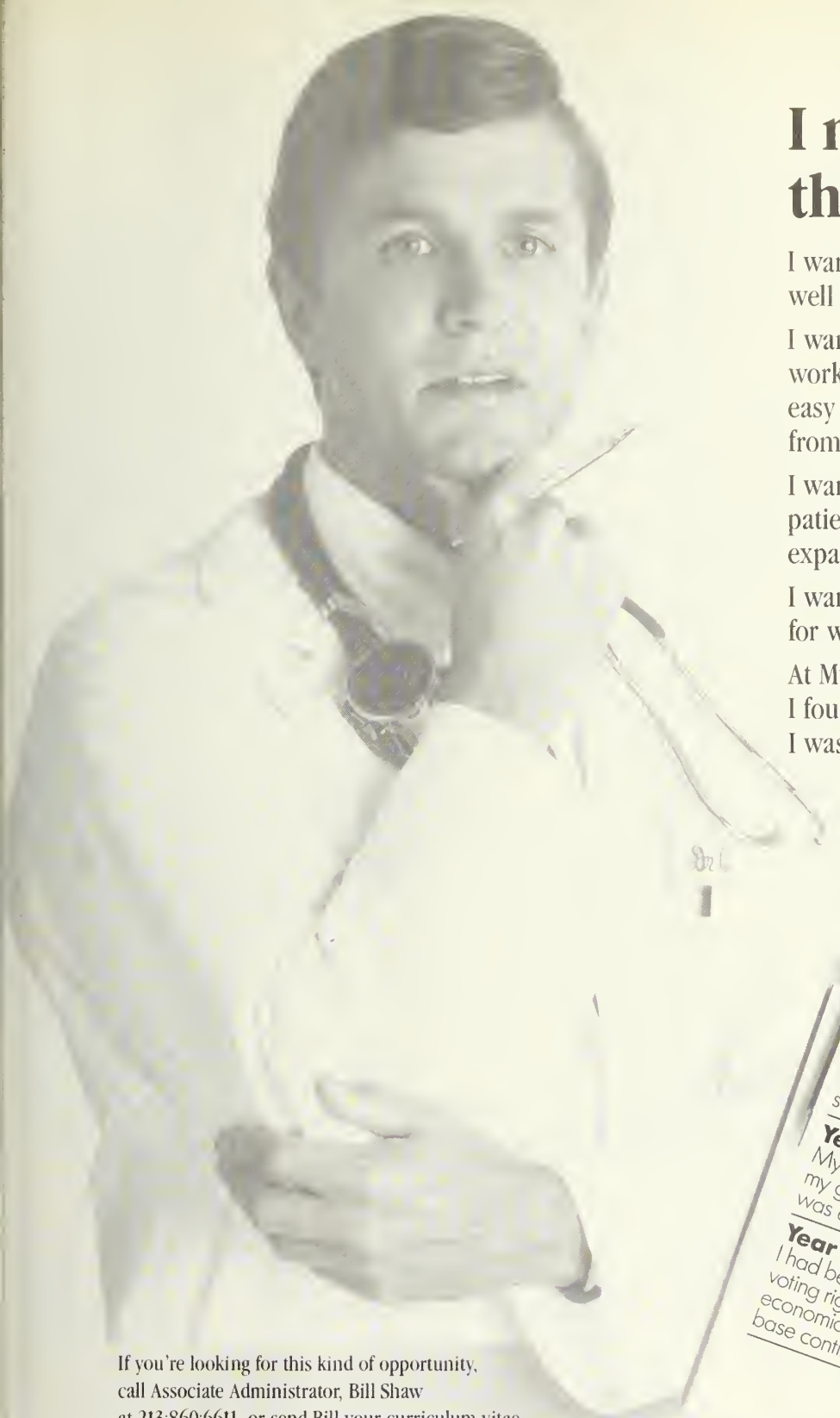
The next step in treatment is to stop AchE totally, even if the clinical impression is that the crisis has not been induced by excessive use of these drugs. The rationale for this latter approach is: first, the continuation of AchE will not help the respiratory muscles as long as the infection remains; second, the continuation of AchE may increase the secretion of upper respiratory tracts which makes suctioning more difficult; and third, as long as the patient is on mechanical ventilation, the discontinuation of AchE is not harmful to the patient. It also is important to keep in mind that patients who are in crisis, and who have an unidentifiable source of infection, may require broad spectrum antibiotics even if they potentially interfere with neuromuscular transmission.

Cephalosporines appear to be a reasonable choice in this situation. After the infection has subsided, and the patient is able to breathe spontaneously, the AchE may be restarted at a slightly lower than maintenance dose, and adjusted according to the patient's clinical response, or according to a Tensilon test.

During crisis, it is usually not necessary to change other medications, such as corticosteroids. When a precipitating factor for the crisis cannot be identified, and the patient is not improving sufficiently after discontinuation of AchE drug, plasmapheresis is very effective for rapid improvement. However, some patients need an increment dose of Prednisone, or cycotoxic agents. In some centers, plasmapheresis is routinely done in patients in crisis without consideration of the cause of precipitating factors. The latter approach, however, is dependent upon the availability of this procedure, cost effectiveness, and, also, trained personnel.

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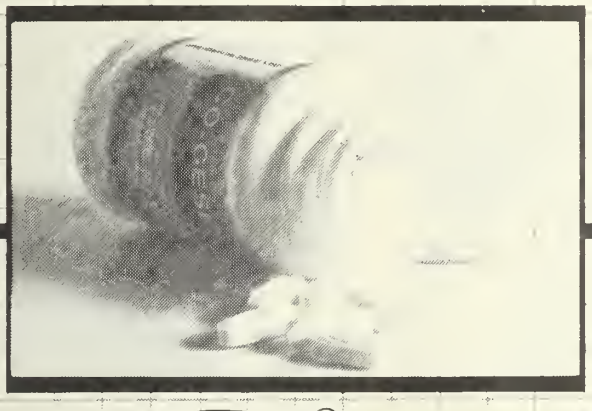
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Anti-Arrhythmic Agents

Update on New Drugs and Their Classification (Part 2)

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Indianapolis

LAST MONTH, the problem of sudden cardiac death was introduced to focus attention on the need for better anti-arrhythmic therapy. A classification scheme to simplify use of anti-arrhythmic agents was proposed. The Class I anti-arrhythmics currently approved for clinical use such as quinidine, procainimide, disopyramide, tocainide, and flecainide were summarized and several newer investigational agents were introduced. This segment focuses on several of the newly released beta blockers, the clinical utility of amiodarone and other Class III anti-arrhythmics, and the usefulness of the calcium channel blocker verapamil in the treatment of ventricular as well as supraventricular tachycardias.

Class II Anti-Arrhythmics: Beta Blockers

Most ventricular arrhythmias are due to re-entry in ventricular tissue without AV node participation. Beta-blockers have been seldom used in the treatment of ventricular tachycardia. They do, however, have significant efficacy in the treatment of those ventricular arrhythmias triggered by excess catacholamine. These include exercise-induced ventricular tachycardia and arrhythmia associated with myocardial ischemia or infarction.[32] Often these latter arrhythmias are due to "triggered automaticity" rather than re-entry, as their initiation and perpetuation is calcium channel and catacholamine dependent rather than sodium channel dependent.[33]

Desirable features of the newer beta blockers include beta-1 selectivity which minimizes bronchospasm; decreased lipophilicity, which minimizes central nervous system penetration; and intrinsic sympathomimetic activity (ISA) in which the beta receptor is slightly stimulated by the agent at rest with the blocking function only readily apparent during exercise or stress. ISA minimizes the resting bradycardia and sense of fatigue associated with beta-blockade therapy while providing the beta blocking effect desired during activity.[34]

Class III Anti-Arrhythmics

Bretylium tosylate is pharmacologically similar to guanethidine but has an additional anti-arrhythmic effect. It is presently approved for use in the United States for intravenous administration in the setting of "refractory" ventricular fibrillation and ventricular tachycardia.[35] Its oral form has been withdrawn from investigators due to the side effects of orthostatic hypotension, gastrointestinal irritation, and parotid gland discomfort when given for extended periods of time. A similar medication, bethanidine sulfate, may have fewer side effects when given orally but maintains similar anti-arrhythmic effects.[36]

Amiodarone was initially utilized in France as an anti-anginal agent. It became recognized as a unique anti-arrhythmic agent which, like bretylium, facilitates treatment of ventricular arrhythmias refractory to Class I anti-arrhythmics.[37-38] The structural formula of amiodarone has two important characteristics: It is a benzofuran derivative and it contains a 37.2% iodine by weight. Amiodarone is metabolized to desethyl-amiodarone and both the parent drug and metabolite are extensively stored in tissues. In fact, the tissue drug concentrations may be 30 to 150 times higher than plasma concentration. As the drug has a half-life of two to nine weeks, a heavy loading dose is necessary to achieve anti-arrhythmic efficacy in less than one week. The prolonged half-life facilitates continued anti-arrhythmic effectiveness if a patient is poorly compliant and allows single day dosing. After cessation of treatment, arrhythmias may not recur for three to six weeks.

Amiodarone prolongs the action potential duration. To a lesser extent it also decreases the amplitude of the action potential and slows the speed of depolarization.[39] The ECG shows bradycardia, prolongation of the PR interval, slight prolongation of the QRS complex and a variable effect on the QT interval. Amiodarone, like quinidine, and other Class IA drugs, may cause significant QT prolongation in susceptible individuals and result in torsade de pointe. Amiodarone slows conduction through an accessory pathway (Bundle of Kent). The anti-arrhythmic effects of amiodarone are complex, and likely related to Class III membrane effects, a weak beta blocking effect, modification of thyroid func-

tion due to its high iodine content, and some degree of sodium channel blockade. Its vasodilating effects may also be important, particularly in individuals with ischemic heart disease. It is also a non-competitive alpha blocker and a weak inhibitor of the calcium channel.

Superficially, amiodarone would seem to have many characteristics of an ideal anti-arrhythmic.[40] It has a long half-life, which facilitates compliance and minimizes the chances of breakthrough tachycardia if a dose is inadvertently omitted. It is also effective in both supraventricular and ventricular arrhythmias. Amiodarone is not useful to convert the patient with atrial fibrillation to normal sinus rhythm but may be used to maintain a patient in sinus rhythm once converted electrically or pharmacologically. Unfortunately, it has significant side effects which limit its application only to life-threatening situations.[40-42] It has been associated with fulminate pulmonary fibrosis causing death, hypothyroidism and hyperthyroidism, corneal microdeposits, silver pigmentation of the skin, sun sensitivity, gastrointestinal side effects, CNS side effects, and neuromuscular toxicity. It also causes hepatic inflammation similar to "alcoholic hepatitis" in all patients to whom it is administered.

Interestingly, amiodarone may also be given intravenously, which results in a different electrophysiologic effect and a more significant negative inotropic effect than when given orally. It does have usefulness in the setting of refractory ventricular arrhythmias when given intravenously.

A reasonable oral loading dose for amiodarone would be 800 mg po q12H for seven days, 800 mg po q.d. x seven days, 400 mg po q.d. x seven days followed by reduction to maintenance dosing. The maintenance dosing is usually 200 mg po daily, but 400 mg or 600 mg per day may be required to control the arrhythmia. In this situation, it is recommended that a second anti-arrhythmic be added rather than continuing high doses of amiodarone for a prolonged period of time. Any of the Class I anti-arrhythmics may be combined with amiodarone but their toxicities may be additive; for example, quinidine may potentiate prolonged QT syndrome whereas flecainide may aggravate the bradyarrhythmia or AV delay.

Assessment of the anti-arrhythmic effect generally requires prolonged continuous monitoring or repetitive Holter monitoring and exercise testing. Some investigators have reported electrophysiologic stimulation testing to be of little benefit in evaluating clinical response to amiodarone.[38] Blood levels also seem to be of less help than with other anti-arrhythmics.[43,44] It has been suggested that reverse thyroid level measurements correlates with clinical efficacy.[40] The development of side effects is dose dependent, with a much higher frequency of side effects observed in individuals receiving an accumulated dose over 1000 grams. It is unusual for serious pulmonary or thyroid complications to develop within the first three to six months of therapy.[45-48] Measurement of pulmonary diffusion capacity correlates with subsequent development of pulmonary fibrosis.[49]

Amiodarone has significant drug interactions.[40] For example, the dose of coumadin must be decreased considerably when beginning amiodarone. The serum digoxin level is elevated by amiodarone. The effects of beta blockade and calcium channel blockade are magnified by amiodarone, particularly the bradycardic effect, AV conduction delay and negative inotropic effect.

It should be recognized that despite its long list of side effects, it is rare to have to discontinue amiodarone because of side effects. Pro-arrhythmic effect has been documented in approximately 15% of individuals beginning amiodarone. Pulmonary fibrosis may occur in approximately 5% and requires temporary withdrawal of the drug or reduction in dosage. Steroid therapy may or may not be indicated, depending upon the severity of the pulmonary disease. Re-institution of amiodarone may be possible following the disappearance of pulmonary infiltrates using a lower dose. Measurement of diffusion capacity in a serial fashion at this time is useful in predicting recurrent pulmonary complications.[49] Hypothyroidism is simply treated with thyroid supplementation and hyperthyroidism may be controlled with the usual drugs. Serious neuromuscular side effects mandate the discontinuation of the medication as permanent neuropathy may result. The corneal deposits rarely interfere with vision and do resolve once the medication is discontinued as do the skin deposits. Photosensitivity may be partially improved by vitamin B6 (pyridoxine) administration and the use of a sun screen. It is rare for the nausea or constipation occasionally seen with amiodarone to require discontinuation.[53]

TABLE 3
Side Effects in 109 Patients Treated with Amiodarone

Corneal Microdeposits	24
Thyroid dysfunction	16
(hyper	11)
(hypo	5)
Photo Sensitivity	11
Gastrointestinal upset	8
Pulmonary toxicity	6
Cardiovascular toxicity	2
(bradycardia	1)
(prolonged QT, proarrhythmic	1)

Since 1982, we have treated 109 patients with amiodarone. A total of 67 have experienced adverse effects as outlined in *Table 3*, yet discontinuation of amiodarone has been necessary in only five individuals due to lack of efficacy (2) or pulmonary toxicity (3). Seventy-four patients continue to show successful suppression of previously refractory ventricular arrhythmia, 67 on amiodarone alone and seven in combination with a second anti-arrhythmic agent: quinidine-4, tocainide-3. Five individuals stopped taking amiodarone: three because of reversible pulmonary toxicity and two because the drug was ineffective. One patient was tapered off amiodarone after 2½ years of therapy without tachycardia recurrence at one year. One other patient underwent cardiac transplantation with concomitant discontinuation of amiodarone. Twenty-eight patients died while taking amiodarone, 12 suddenly, 10 with refractory congestive heart failure, two with cancer (lung, breast), one with necrotizing pancreatitis after coronary by-pass surgery, two with refractory sepsis (aspiration pneumonia, urinary tract), and one in an automobile accident. Amiodarone was discontinued in six patients for appearance of pulmonary infiltrates but could be restarted in three of these individuals at a lower dose at a later time without recurrent pulmonary problems.

It may be seen, from our experience as well as that of other investigators, that amiodarone is a particularly potent oral anti-arrhythmic for refractory ventricular arrhythmias. It has, unfortunately, serious side effects which demand close follow-up observation on a monthly basis during this first year of therapy and later follow-up intervals no longer than every three months. Appropriate laboratory testing, especially thyroid function and hepatic function tests, are required along with serial chest x-rays. At no time should amiodarone be used for "simple" VPCs unassociated with "complex" or malignant arrhythmia grades.

NAPA (n-acetyl procainamide) is the primary metabolite of procainamide. Recently it has been recognized that it has potent anti-arrhythmic effects which differ from those of the parent compound.[54] NAPA increases the effective refractory period and the QT and QTc intervals without altering the conduction time or decreasing automaticity. Its effects, therefore, are more similar to bretylium than procainamide. Also, like bretylium, it increases contractility rather than being a negative inotrope like procainamide. The half-life is longer than procainamide, permitting BID dosing. It has a low incidence of side effects and a markedly decreased incidence of drug-induced lupus. The major adverse effects of NAPA are nausea, blurred vision, headaches, constipation, fatigue, impotence and insomnia. Rarely, patients may develop positive ANA and arthralgias, probably due to the reverse conversion of NAPA to small amounts of procainamide. Rare cases of Coomb's positive hemolytic anemia have been reported.

Sotalol is a non-selective beta adrenergic blocking agent with the additional property of producing prolongation of duration of the cardiac action potential.[55] Therefore, it shares both Class II and Class III anti-arrhythmic activity. The side effects of sotalol are similar to those of other beta blockers.

Class IV Anti-Arrhythmics: Calcium Channel Blockers

Verapamil: Although all the calcium channel blockers have *in vitro* negative chronotropic and dromotropic effects, only verapamil and, to a lesser extent, diltiazem, are useful in the treatment of supraventricular arrhythmias, primarily by slowing conduction through the AV node.

Verapamil is available intravenously and has become the drug of choice for slowing or terminating supraventricular arrhythmias with antegrade conduction through the AV node. It is relatively contraindicated if an accessory pathway participates in the tachycardia as it may speed conduction through the Bundle of Kent. Both verapamil and diltiazem may be useful for chronic oral administration to prevent the occurrence or minimize the rate of certain supraventricular arrhythmias. Verapamil has been shown useful in certain ventricular tachycardias due to "triggered automaticity" rather than re-entry.[56]

Triggered automaticity refers to a phenomenon occurring when a single cell or groups of cells become partially depolarized due to ischemia or electrolyte imbalance and hence develop intrinsic rhythmicity due to the calcium channel rather than the inactivated sodium channel. These arrhythmias are often aggravated by an increase in heart rate or increase in catacholamine level. As they are calcium current dependent in the setting of inactivated sodium channel, the Class I anti-arrhythmics (which are sodium channel blockers) show little or no efficacy. In electrophysiologic testing a small number (approximately 7%) of inducible ventricular tachycardias may be ascribed to triggered automaticity. For this reason, when the usual agents fail in the treatment of ventricular tachycardia, consideration for treatment with verapamil is appropriate.

The usual dose of verapamil for supraventricular and ventricular arrhythmias is 5 mg given intravenously over two minutes followed by a second 5 mg three minutes later if no effect on the arrhythmias is noted. Close attention to both heart rate and blood pressure is necessary as verapamil may be a potent negative inotrope, especially in the setting of pre-existent left ventricular dysfunction or concomitant beta blocking therapy. Beta blockers slow hepatic blood flow and, because verapamil is totally metabolized in the liver, cause very high verapamil levels when concomitantly administered. When given orally, verapamil often causes chronic constipation. Verapamil elevates the digoxin level when simultaneous administration is undertaken and there-

fore the dose of digoxin should be halved at the time of beginning verapamil therapy.

Verapamil may be used in combination with any of the other antiarrhythmics, but attention must be paid to bradyarrhythmias and negative inotropic effect when combined with disopyramide, Class IC or II agents and/or amiodarone. The side effects of verapamil and quinidine often "cancel out" when combined, particularly with reference to the gastrointestinal disorders. The combination of quinidine and verapamil is particularly efficacious in treating paroxysmal atrial fibrillation with rapid ventricular response. Finally, as verapamil has little of the depression, impotence, fatigue or memory loss associated with chronic beta blockade therapy, it becomes particularly useful in young individuals who require chronic antiarrhythmic therapy.

Conclusion

A clinically useful classification scheme for a variety of anti-arrhythmic agents has been outlined. These pharmaceuticals have improved our ability to treat ventricular ectopy while minimizing side effects. Nevertheless, the problem of sudden cardiac death remains a serious and prevalent one. While the future promises antitachycardia pacemaker devices including implantable defibrillators, the cost of these tools and their invasiveness will limit their applicability.[57-59] We desperately require a noninvasive measure of electrical instability to better predict both the need for and efficacy of anti-arrhythmic agents.[60-62] This will be a major challenge facing cardiologists in the 1990s.

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In two randomized, double-blind, and well-controlled clinical trials, ZANTAC 150 mg h.s. significantly superior to cimetidine 400 mg h.s. for maintenance therapy in healed duodenal ulcers.

Percent of patients with observed duodenal ulcer recurrence

		0-4 months	0-8 months	0-12 months	No. patients
USA[1]	ranitidine 150 mg h.s.	9%	14%*	16%†	60
	cimetidine 400 mg h.s.	23%	34%	43%	66
UK, Ireland, Australia[2]	ranitidine 150 mg h.s.	8%‡	14%‡	23%‡	243
	cimetidine 400 mg h.s.	21%	34%	37%	241

*p=0.02
†p=0.01
‡p≤0.004
%=life-table estimates
All patients were permitted prn antacids for relief of pain.

These two trials used the currently recommended dosing regimen of cimetidine (400 mg h.s.) and ranitidine (150 mg h.s.). A comparison of other dosing regimens has not been studied.

The studied dosing regimens are not equivalent with respect to the degree and duration of acid suppression or suppression of nocturnal acid.

The superiority of ranitidine over cimetidine in these trials indicates that the dosing regimen currently recommended for cimetidine is less likely to be as successful in maintenance therapy.

Convenient once-a-night dose with a

low incidence of side effects[3]

Headache, sometimes severe, seems to be related to ranitidine administration. Other side effects have been reported; for a complete listing, see the **ADVERSE REACTIONS** section in the Brief Summary.

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ZANTAC 150 mg has no significant drug interactions with theophylline, phenytoin, or warfarin. The bioavailability of certain medications whose absorption is dependent on a low gastric pH may be altered when ZANTAC or other medications that decrease gastric acidity are administered.

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See next page for references and
Brief Summary of Product Information.

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References:

1. Silvis SE, Griffin J, Hardin R, et al: Final report on the United States multicenter trial comparing ranitidine to cimetidine as maintenance therapy following healing of duodenal ulcer. *J Clin Gastroenterol* 1985;7(6):482-487.
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3. Data available on request, Glaxo Inc.

ZANTAC® 150 Tablets
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ZANTAC® 300 Tablets
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BRIEF SUMMARY OF PRODUCT INFORMATION

The following is a brief summary only. Before prescribing, see complete prescribing information in ZANTAC® product labeling.

INDICATIONS AND USAGE: ZANTAC® is indicated in:

1. Short-term treatment of **active duodenal ulcer**. Most patients heal within four weeks.
2. **Maintenance therapy** for duodenal ulcer patients at reduced dosage after healing of acute ulcers.
3. The treatment of **pathological hypersecretory conditions** (eg, Zollinger-Ellison syndrome and systemic mastocytosis).
4. Short-term treatment of **active, benign gastric ulcer.** Most patients heal within six weeks and the usefulness of further treatment has not been demonstrated.
5. Treatment of **gastroesophageal reflux disease (GERD)**. Symptomatic relief commonly occurs within one or two weeks after starting therapy and is maintained throughout a six-week course of therapy.

In active duodenal ulcer; active, benign gastric ulcer; hypersecretory states; and GERD, concomitant antacids should be given as needed for relief of pain.

CONTRAINDICATIONS: ZANTAC® is contraindicated for patients known to have hypersensitivity to the drug.

PRECAUTIONS: Symptomatic response to ZANTAC® therapy does not preclude the presence of gastric malignancy.

Since ZANTAC is excreted primarily by the kidney, dosage should be adjusted in patients with impaired renal function (see **DOSAGE AND ADMINISTRATION**). Caution should be observed in patients with hepatic dysfunction since ZANTAC is metabolized in the liver.

False-positive tests for urine protein with Multistix® may occur during ZANTAC therapy, and therefore testing with sulfosalicylic acid is recommended.

Although recommended doses of ZANTAC do not inhibit the action of cytochrome P-450 enzymes in the liver, there have been isolated reports of drug interactions which suggest that ZANTAC may affect the bioavailability of certain drugs by some mechanism as yet unidentified (eg, a pH-dependent effect on absorption or a change in volume of distribution).

Lack of experience to date precludes recommending ZANTAC for use in children or pregnant patients. Since ZANTAC is secreted in human milk, caution should be exercised when administered to a nursing mother.

ADVERSE REACTIONS: Headache, sometimes severe, seems to be related to ZANTAC® administration. Constipation, diarrhea, nausea/vomiting, and abdominal discomfort/pain have been reported. There have been rare reports of malaise, dizziness, somnolence, insomnia, vertigo, tachycardia, bradycardia, premature ventricular beats, and arthralgias. Rare cases of reversible mental confusion, agitation, depression, and hallucinations have been reported, predominantly in severely ill elderly patients.

In normal volunteers, SGPT values were increased to at least twice the pretreatment levels in 6 of 12 subjects receiving 100 mg qid IV for seven days, and in 4 of 24 subjects receiving 50 mg qid for five days. With oral administration there have been occasional reports of reversible hepatitis, hepatocellular or hepatocanalicular or mixed, with or without jaundice.

There have been rare reports of reversible leukopenia, granulocytopenia, thrombocytopenia, and pancytopenia.

Although controlled studies have shown no antiandrogenic activity, occasional cases of gynecomastia, impotence, and loss of libido have been reported in male patients receiving ZANTAC, but the incidence did not differ from that in the general population.

Incidents of rash, including rare cases suggestive of mild erythema multiforme, and, rarely, alopecia, have been reported, as well as rare cases of hypersensitivity reactions (eg, bronchospasm, fever, rash, eosinophilia) and small increases in serum creatinine.

OVERDOSAGE: Information concerning possible overdosage and its treatment appears in the full prescribing information.

DOSAGE AND ADMINISTRATION Active Duodenal Ulcer: The current recommended adult oral dosage is 150 mg twice daily. An alternate dosage of 300 mg once daily at bedtime can be used for patients in whom dosing convenience is important. The advantages of one treatment regimen compared to the other in a particular patient population have yet to be demonstrated.

Maintenance Therapy: The current recommended adult oral dosage is 150 mg at bedtime.

Pathological Hypersecretory Conditions (such as Zollinger-Ellison Syndrome): The current recommended adult oral dosage is 150 mg twice a day. In some patients it may be necessary to administer ZANTAC 150-mg doses more frequently. Doses should be adjusted to individual patient needs, and should continue as long as clinically indicated. Doses up to 6 g/day have been employed in patients with severe disease.

Benign Gastric Ulcer: The current recommended adult oral dosage is 150 mg twice a day.

GERD: The current recommended adult oral dosage is 150 mg twice a day.

Dosage Adjustment for Patients with Impaired Renal Function: On the basis of experience with a group of subjects with severely impaired renal function treated with ZANTAC, the recommended dosage in patients with a creatinine clearance less than 50 ml/min is 150 mg every 24 hours. Should the patient's condition require, the frequency of dosing may be increased to every 12 hours or even further with caution. Hemodialysis reduces the level of circulating ranitidine. Ideally, the dosage schedule should be adjusted so that the timing of a scheduled dose coincides with the end of hemodialysis.

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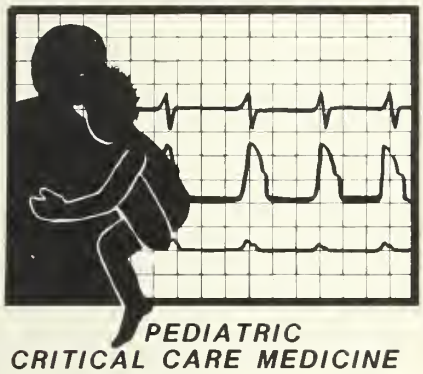
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Pediatric Heatstroke: A Case Report



PEDIATRIC
CRITICAL CARE MEDICINE

Methodist Hospital of Indiana, Inc.

STEPHEN K. NUGENT, M.D.
Indianapolis

HEATSTROKE IS THE most severe manifestation of a clinical spectrum of heat-related illnesses. The following case is that of a child with heatstroke who presented at an age not usually associated with this extreme medical emergency.

Case Report

A 7-year-old obese boy developed fever, lethargy, and unintelligible speech on a hot (98° F) and humid (90%) August day. Vomiting and diarrhea from gastroenteritis treated with Donnatal (phenobarbital and anticholinergic) preceded this change in mental status. After a long van ride, which included a brief stop at a physician's office, he presented to an emergency department where his admitting rectal temperature was 108° F. He was unresponsive (Glasgow Coma Score 4) with dilated and nonreactive pupils. Minimal sweating was noted. Physostigmine did not improve mental status or pupillary response. Ice water bath cooling resulted in a rectal temperature of 100.5° F two hours after presentation. He remained unresponsive and hypotensive. Four hours after presentation and just prior to helicopter transport his temperature was 86° F.

Upon arrival at the Pediatric Intensive Care Unit, his pulse was 136, respirations 30, rectal temperature 97° F, and his systemic blood pressure unobtainable. He remained flaccid and areflexic with dilated and nonreactive pupils. Vomiting and liquid stools occurred repeatedly. He was intubated, fluid resuscitated, and continuous infusions of both dopamine (30 mcg/kg/min) and norepinephrine (0.2 mcg/kg/min) were begun. Additional venous, and systemic arterial and pulmonary artery catheters were placed. Movement to pain and pupillary reaction returned when a mean blood pressure of 60 mm HG was obtained.

Two hours after admission, the temperature had risen to 102° F. A generalized seizure was treated with Valium and Dilantin. Urine output began after furosemide, mannitol, and establishment of an adequate blood pressure. Fresh frozen plasma and Vitamin K were given in response to nasogastric tube and cutdown site bleeding and a prolonged prothrombin time. Other abnormal lab values included a BUN of 54 mg/dL, serum creatinine 2.9 mg/dL, serum glucose 61 mg/dL, and serum bicarbonate 17 mEQ/L. Pulmonary artery catheterization data after initial fluid resuscitation revealed an above normal left ventricular preload, depressed ventricular contractility, below normal systemic vascular resistance, and a cardiac output slightly above normal. Ongoing hemodynamic profile data guided both fluid and catecholamine administration.

On the day following admission, the patient responded to commands. Mean blood pressure was 75-82 mm HG on decreased amounts of dopamine (15 mcg/kg/min) and norepinephrine (0.1 mcg/kg/min). Peripheral pulses were normal, and urine output (without myoglobin) excellent. Almost 10 liters of fluid had been infused during the first 24 hours. Laboratory values included a BUN of 33 mg/dL, creatinine 1.9 mg/dL, platelet count 49,000 (293,000 at admission), SGOT 108 IU/L (n. 8-40), and prolonged prothrombin time without clinical bleeding. Arterial lactic acid was high normal at 1.7

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millimoles/L (not obtained at admission). Parenteral nutrition was begun.

Three days after admission catecholamines had been discontinued and the patient was extubated. Nine days after admission the patient was discharged. Liver function studies had returned to normal. The patient and family were advised of a possible predisposition to subsequent heat intolerance.[1]

Discussion

Essential requirements for the diagnosis of heatstroke include elevated body temperature (usually 105° F/40.6°C or more rectal), central nervous system dysfunction characterized by bizarre behavior, confusion, seizures, or coma, and exposure to heat stress whether environmental or internally generated.[2-5] Most cases of heatstroke, and at least 80% of heatstroke mortality, occur in the elderly and infirm. So-called "classic" heatstroke is seen in epidemics during a well established heat wave.[6] A chronic underlying disease, lack of access to a cool, air-conditioned environment, and medication usage (especially phenothiazines, anticholinergics, diuretics, and beta blockers among many others) are the most well known of many predisposing risk factors.[7]

Infants are also predisposed to classic heatstroke and heat-aggravated illness. A greater ratio of body surface area to mass may result in a greater transfer of heat between the body and environment. Metabolic rate and production of heat per unit of body surface area peaks at about five months while heat loss through sweating develops more slowly over the first year. Preventable infant deaths from heatstroke have resulted from exposure to excessive ambient heat in a closed automobile parked in direct sunlight.[8] An interior temperature of 149° F may be reached in 15 minutes in a car parked in the sun with windows closed and an outside temperature of 96.8° F.[9] Deaths from heatstroke have also been reported in infants 3-8 months old with mild illnesses who were excessively wrapped and externally warmed.[10] The primary versus secondary role of hyperpyrexia in the pathophysiology of the recently described syndrome of acute hemorrhagic shock and encephalopathy (HSES) is yet to be determined.[11] Previously healthy infants suddenly developed severe shock, encephalopathy, hyperthermia, and disseminated intravascular coagulation. Severe neurologic sequelae or death usually resulted.

"Exertional" heatstroke typically occurs in the young unacclimatized athlete, military recruit, or worker exercising in a hot and humid environment. Heat is produced by muscular work at a rate that exceeds the body's capacity to dissipate it. Simple radiation, convection, and conduction become ineffective mechanisms of heat dissipation at high ambient temperature. As relatively humidity rises, evaporative heat loss by sweating also becomes ineffective. The combination of adverse environmental temperature and humidity, strenuous activity, and fluid deficit from sweating and inadequate intake results in inadequate heat dissipation and a rapid rise in core temperature. Resultant tissue and cellular damage is a function of the interaction of body temperature, exposure time, workload, tissue perfusion, and variable individual resistance. It would be difficult to overestimate the role that pediatricians and family physicians can plan in the prevention of heat disorders in sports and in exercising children generally.[12,13]

Space does not allow an in-depth discussion of the clinical manifestations of hyperthermia, many of which were demonstrated by the patient described. Heatstroke is clearly a multi-organ system disease. Shock of a variable nature, central nervous system dysfunction and permanent sequelae, coagulopathy, renal failure, rhabdomyolysis, hepatocellular necrosis, and multiple metabolic abnormalities are common.[2-5,14,15]

Heatstroke mortality is a function of degree and duration of hyperthermia; hence, of delay in restoring core temperature is normal. Survival of the patient described was most directly related to the rapidity with which his temperature was lowered at the outlying hospital. Two major techniques of rapid cooling have been advocated when treating a heatstroke victim whose temperature is above 106° F (41° C).[16] Ice water bath immersion is the traditional method. This method depends upon conduction (direct transfer of heat to another object) as the major means of heat dissipation. An alternative technique relies upon convection (transfer of heat to circulating fluid or gas) and evaporation. The skin is kept wet with tepid water and dry room air from a fan is continually directed at the patient. Regardless of which technique is used, it is important to frequently record core body temperature during cooling and thereafter. Hypothermia can be avoided if cooling measures are discontinued at 102°-103° F. A rebound increase in temperature at 2-6 hours is common, as is several days of thermoregulatory instability, all demonstrated by the patient described.

Other therapeutic modalities include airway protection, adequate intravenous access, supplemental oxygen, careful vital sign monitoring, and control of seizures and muscular hyperactivity. Urine output must be closely monitored. Rhabdomyolysis and myoglobinuria may occur whether heatstroke is exertional or classic.[14] Fluid requirements vary depending upon degree of dehydration and hypovolemia, hypotension, and blood pressure/peripheral vascular resistance response to cooling. Cardiac filling pressure measurement, i.e., central venous or pulmonary artery occluded pressure, may be required to guide fluid administration. If a patient remains hypotensive after both cooling and 15-20 ml/kg of D_5W lactated Ringer's solution, and especially if catecholamine blood pressure support is required, a pulmonary artery catheter is

indicated to guide further therapy. Laboratory metabolic and hematologic assessment is an initial priority. Arterial blood gases must be temperature-corrected for most accurate assessment of oxygenation, ventilation, and acid-base status.[14]

Classic heatstroke in the boy described above occurred at an unusual age. Chronic illness associated with childhood heat-related illness, e.g., cystic fibrosis, ectodermal dysplasia, diabetes mellitus, familial dysautonomia, etc., was absent. Identifiable predisposing factors, however, included an infection (gastroenteritis) with preexisting fever, dehydration, obesity, and use of anticholinergic medication which inhibits sweating and heat dissipation.

All heatstroke literature cautions against the use of norepinephrine, a potent alpha agonist vasoconstrictor, in the management of hypotension. Pharmacologic vasoconstriction may impede heat loss. Given the patient's normal core temperature in the Pediatric Intensive Care Unit, the profound hypotension despite adequate fluid resuscitation and preload (pulmonary artery occlusion pressure), and a measured low systemic vascular resistance and above normal cardiac output, alpha agonist blood pressure support was indicated. This case is an excellent example of how fluid/catecholamine administration, based upon pulmonary artery catheter data, can optimize the determinants of cardiac output and blood pressure.

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THE FAITH ASSEMBLY

A Follow-up Study of Faith Healing and Mortality

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Abstract

We investigated births and deaths within an Indiana religious group that was avoiding all medical care, including prenatal services. Religious group perinatal and maternal mortality rates for the years 1983-1985 were sharply lower than they were for the years 1975-1982. These findings suggest that public health and legal surveillance have an important role in the prevention of medical neglect.

SPIRITUAL "FAITH HEALING" as an alternative to medical care has long been a subject of discussion, particularly with respect to child abuse and neglect issues.[1]

In March 1984, the Indiana State Board of Health and the Division of Reproductive Health of the Centers for Disease Control published a study of maternal and perinatal deaths in a "charismatic" religious group avoiding all medical and obstetrical care.[2]

The Faith Assembly, active in Indiana since 1973 with about 2,000 members, resides predominantly in Elkhart and Kosciusko Counties and creates the opportunity to examine the effects on mortality of avoiding medical care. The pilot study, the first investigation of maternal and perinatal mortality rates for a religious group in the U.S.,[3] revealed a perinatal mortality rate three times higher than for Indiana statewide ($p < 0.001$) and a maternal mortality about 100 times higher than the remainder of the state ($p < 0.0001$).[2,4,5]

Following these publications and associated nationwide media coverage, the Indiana General Assembly revised the child abuse/neglect statute to require the reporting of withheld medical care—even if the parents object for religious reasons. Late in 1984, the first of nine Indiana Faith Assembly parents were convicted for allowing their child's death without benefit of medical care. On May 27, 1986, the Indiana Supreme Court upheld an original conviction of reckless homicide—parents who offered prayer without medicine, causing the death of their infant son to pneumonia. Another couple is scheduled to stand trial in Elkhart County.

Faith Assembly doctrine has forbidden members to seek medical attention for any health problem; however, the charismatic leader of the sect has died—of "treatable" disease—and local authorities now suspect that followers may be seeking health services.

Following completion of the pilot study, the Vital Records and Maternal and Child Health Divisions of the Indiana State Board of Health invited the cooperation of the Elkhart and Kosciusko County health departments to maintain surveillance for further Faith Assembly birth/death occurrences. Data acquired from 1983 through 1985 is the subject of this study.

Methods

Between 1983 and 1985, birth and death certificates were manually screened by local health officials in Kosciusko and Elkhart Counties and forwarded monthly to the State Board of Health. Birth certificates were identified as Faith Assembly according to the following criteria: out-of-hospital birth, unlicensed birth attendant, zero prenatal visits, no serology or ophthalmia neonatorum prophylaxis, religious or personal reasons for the above cited, and legitimate birth. Death certificates were identifable according to the same criteria and manually matched to birth records. Further information was provided by local investigative news reporters.

Perinatal mortality rates were calculated for Faith Assembly in Kosciusko and Elkhart Counties and compared to statewide rates. These rates were then compared to those for the years 1975 through 1982. The perinatal mortality rate is defined as the number of neonatal deaths (death $\leq$28 days after birth) and fetal deaths ($\leq$20 weeks gestation) per 1,000 live births plus fetal deaths.

Deaths in other age groups were also identified, including maternal deaths. Causes of death were documented where possible by autopsy results.

Exact methods were used to

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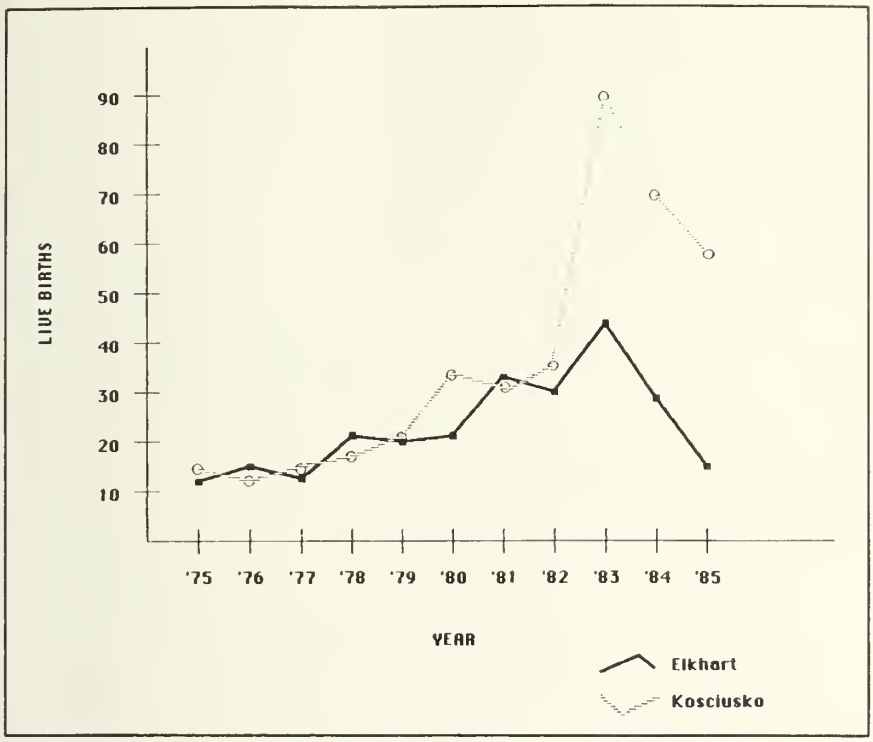


FIGURE 1: Faith Assembly live births, Elkhart and Kosciusko Counties, 1975 through 1985.

calculate statistical significance and 90% confidence intervals.

Certain characteristics obtainable from birth records, including age of mother, educational status, and parity, were compared with other Indiana women.

Results

Identified were 314 Faith Assembly live births in Elkhart and Kosciusko Counties from 1983 through 1985, compared to 344 Faith Assembly births from 1975 through 1982. As shown in *Figure 1*, birth numbers peaked in 1983 and have subsequently fallen.

Eight perinatal deaths (5 fetal, 3 neonatal) occurred from 1983-1985 (*Figure 2*) as compared to 17 (11 fetal, 6 neonatal) from 1975-1982.[2,4]

As shown in *Table 1*, the estimated perinatal mortality rate for the years 1983 through 1985 for Faith Assembly members residing in Elkhart and Kosciusko Counties was 25.1 deaths per 1,000 live births, declining from 47.9 deaths per 1,000 live births between 1975 and 1982 (90% confidence limits, $p < 0.10$).

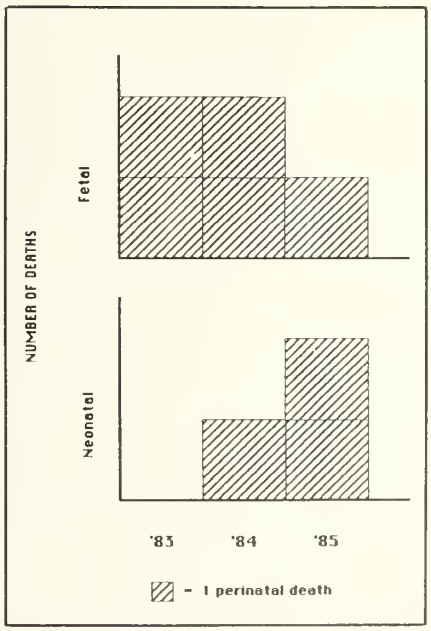


FIGURE 2: Faith Assembly perinatal deaths, Elkhart and Kosciusko Counties, 1983 through 1985.

There were no Faith Assembly maternal deaths reported between 1983 and 1985. Of interest, there were three infant deaths (two of pneumonia, and one of meningitis, two adolescent deaths (renal failure in one and untreated diabetes in the other), and three non-maternal adult deaths (including the founder of the sect).—*Table 2*.

Faith Assembly women were particularly parous as compared with other Indiana women, 56% having four or more pregnancies versus 9%; most were 20-34 years of age (see *Table 3*); and educational attainment was high—53% with more than a high school education.

"Lack of medical care" or "complications of prematurity and/or childbirth" were identifiable factors in all Faith Assembly perinatal deaths.

Discussion

Between 1975 and 1982 the estimated perinatal and maternal mortality rates for Faith Assembly were about three-fold and 100-fold higher, respectively, than statewide rates.[4] Since 1983, however, the perinatal mortality rate has declined to 1.5 times the rate for the rest of Indiana. Maternal mortality has been eliminated, despite the relatively large numbers of births.

Increasing numbers of out-of-hospital births are occurring with "religious" attachments and, significantly, prenatal visits documented on the birth certificate. This would suggest Faith Assembly women may be seeking, at least partially, reproductive health care.

There has been no evidence since 1983 that Faith Assembly members have attempted to hide perinatal deaths, although one perinatal death was identified for which no birth certificate was filed.

The dramatic death statistics demonstrated for the years 1975

TABLE 1
Average Perinatal Mortality Rates,
Kosciusko and Elkhart County
Faith Assembly and Indiana Statewide,
1975-1985

	1975-85	1983-85
Faith Assembly	47.9	21.9
Indiana Statewide	17.8	14.7

PMR = Deaths per 1,000 live births

TABLE 3
Selected Characteristics of Faith Assembly
and Other Indiana Women, 1983 through 1985

CHARACTERISTICS	FAITH ASSEMBLY (%)	INDIANA (%)
Age 20-34 Years	90	90
Parity ≥ 4	56	8.6
Legitimacy	100	81

through 1982, intervention by the Indiana General Assembly, and willingness of local prosecutors to intervene on behalf of the Faith Assembly children, all have contributed to the apparent decline in perinatal and maternal mortality. Changes in leadership signalled by the death of the Faith Assembly founder may also have had some effect.

We as public health officials remain profoundly concerned about preventable deaths, injuries, and illnesses in other age groups, however, indicating the need for continued surveillance. Alert reporting by school officials has allowed some Faith Assembly children access to medical care for fractures, communicable diseases, and other treatable disorders.[6]

Prayer in support of patients under medical treatment or in support of those whom medical science cannot help is outside of the state's realm of comment. Public health officials will, however, continue to provide a dual responsibility to the state and its young patients, intervening on their behalf and discouraging medical neglect.

TABLE 2
Faith Assembly Deaths,
Elkhart and Kosciusko Counties, 1975 through 1985,
According to Age Group

	1975-82	1983	1984	1985
Fetal (≥20 week gestation)	11	2	2	1
Neonatal (≤28 days)	6	0	1	1
Infant (≤1 year)	2	1	2	0
Children (>1 year)	4	0	1	1
Maternal Adult	3	0	0	0
Non-Maternal Adult	4	0	3	0

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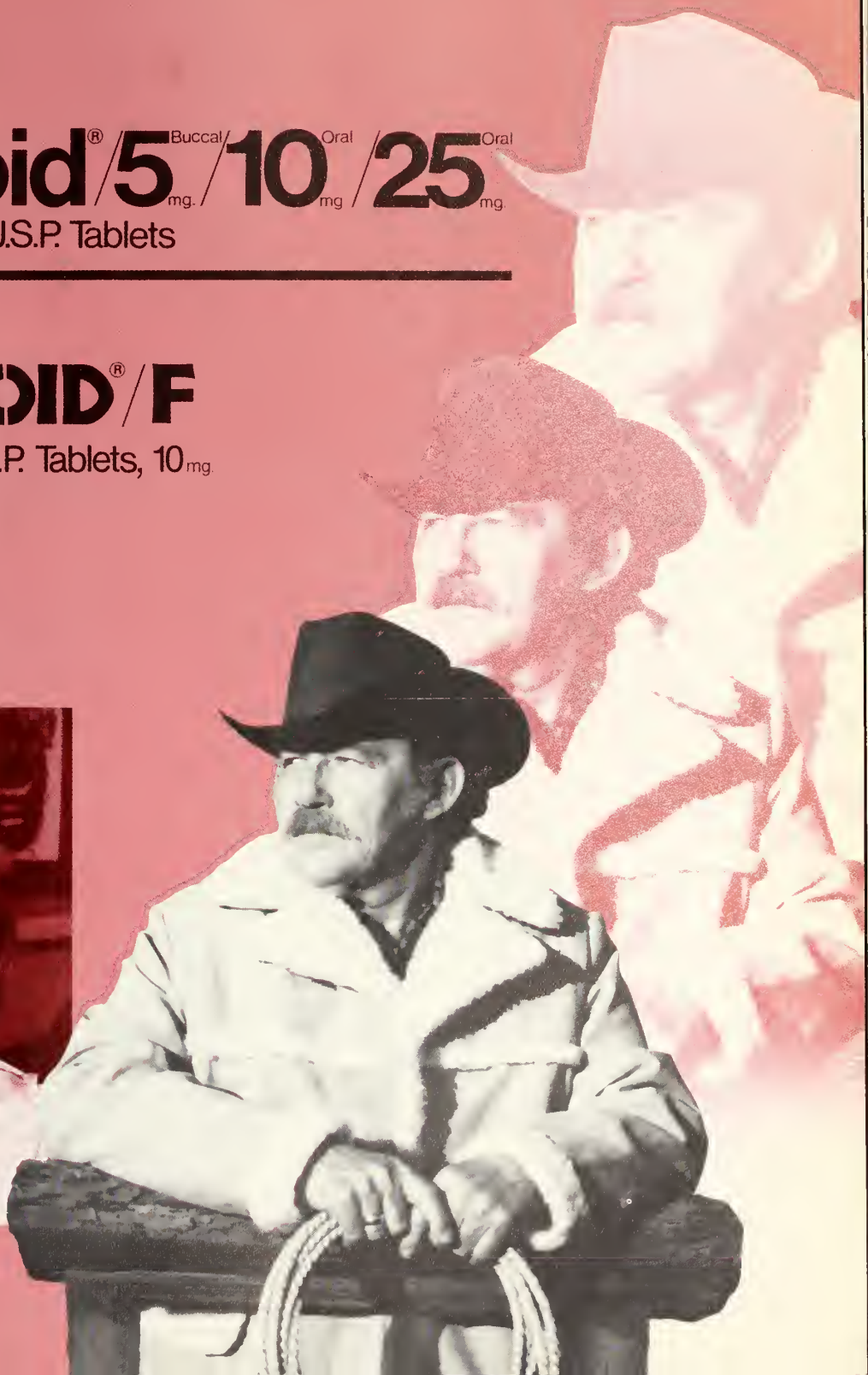
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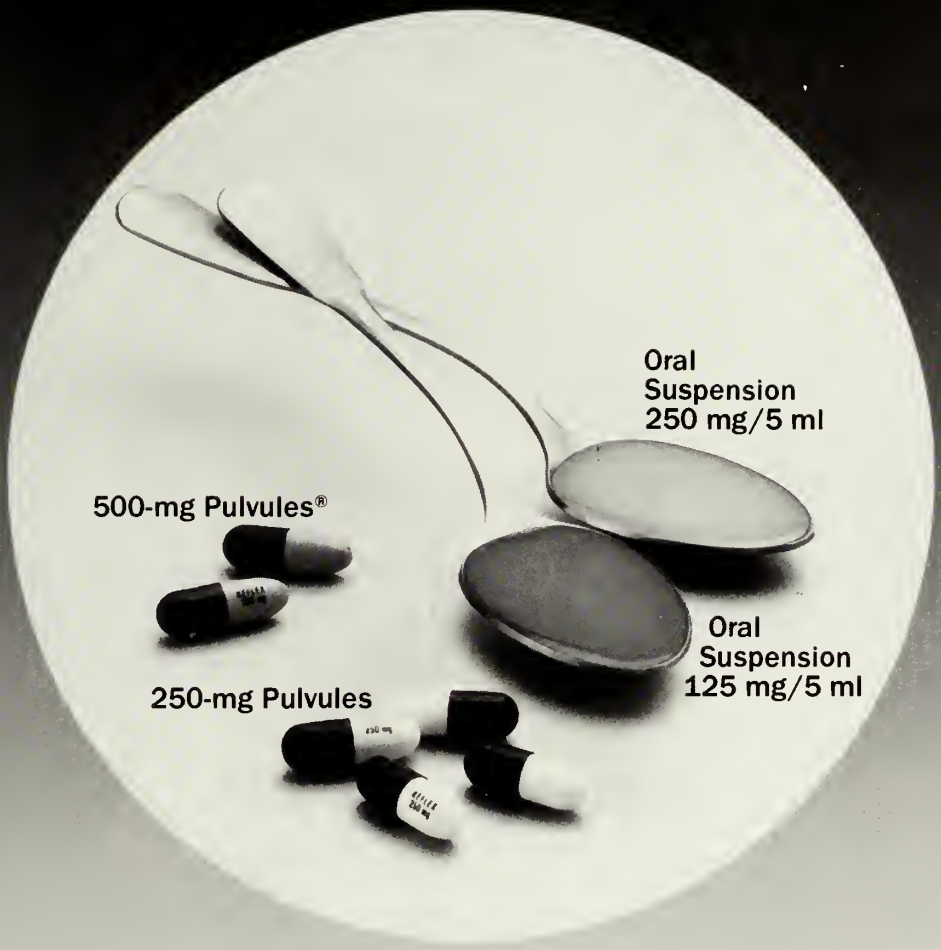
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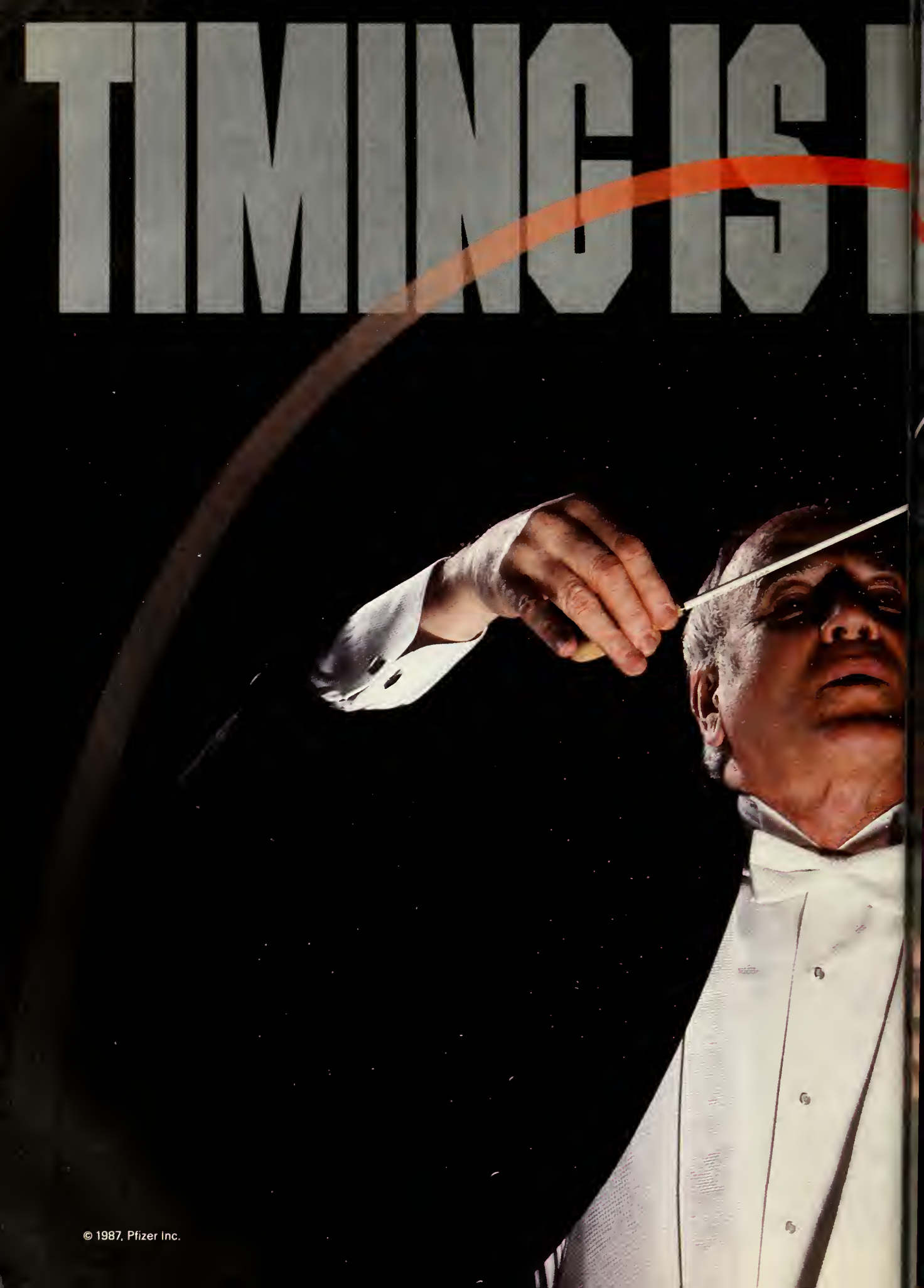
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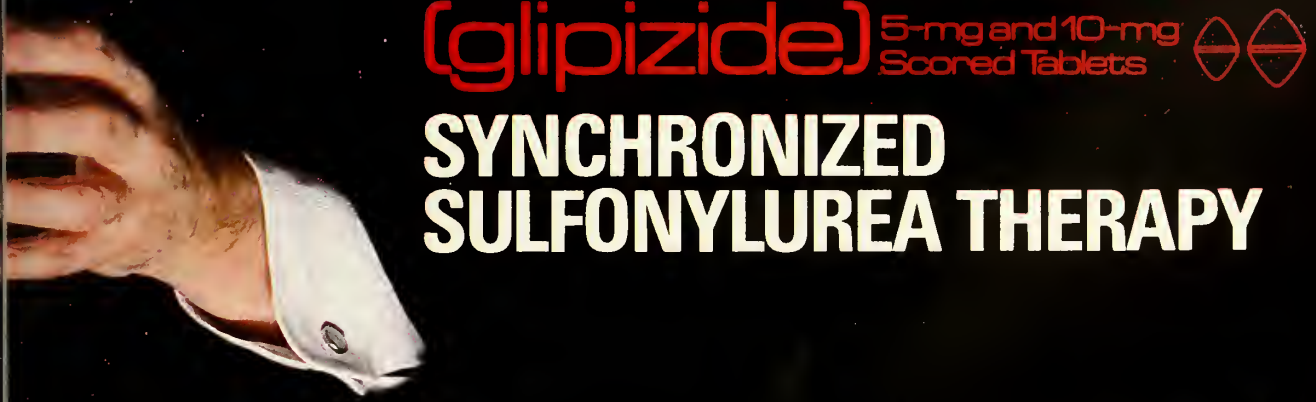
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INDICATIONS AND USAGE: GLUCOTROL is indicated as an adjunct to diet for the control of hyperglycemia in patients with non-insulin-dependent diabetes mellitus (NIDDM, type II) after an adequate trial of dietary therapy has proved unsatisfactory.

CONTRAINDICATIONS: GLUCOTROL is contraindicated in patients with known hypersensitivity to the drug or with diabetic ketoacidosis, with or without coma, which should be treated with insulin.

SPECIAL WARNING ON INCREASED RISK OF CARDIOVASCULAR MORTALITY: The administration of oral hypoglycemic drugs has been reported to be associated with increased cardiovascular mortality as compared to treatment with diet alone or diet plus insulin. This warning is based on the study conducted by the University Group Diabetes Program (UGDP), a long-term prospective clinical trial designed to evaluate the effectiveness of glucose-lowering drugs in preventing or delaying vascular complications in patients with non-insulin-dependent diabetes. The study involved 823 patients who were randomly assigned to one of four treatment groups (*Diabetes*, 19, supp. 2:747-830, 1970).

UGDP reported that patients treated for 5 to 8 years with diet plus a fixed dose of tolbutamide (1.5 grams per day) had a rate of cardiovascular mortality approximately 2-1/2 times that of patients treated with diet alone. A significant increase in total mortality was not observed, but the use of tolbutamide was discontinued based on the increase in cardiovascular mortality, thus limiting the opportunity for the study to show an increase in overall mortality. Despite controversy regarding the interpretation of these results, the findings of the UGDP study provide an adequate basis for this warning. The patient should be informed of the potential risks and advantages of GLUCOTROL and of alternative modes of therapy.

Although only one drug in the sulfonylurea class (tolbutamide) was included in this study, it is prudent from a safety standpoint to consider that this warning may also apply to other oral hypoglycemic drugs in this class, in view of their close similarities in mode of action and chemical structure.

PRECAUTIONS: Renal and Hepatic Disease: The metabolism and excretion of GLUCOTROL may be slowed in patients with impaired renal and/or hepatic function. Hypoglycemia may be prolonged in such patients should it occur.

Hypoglycemia: All sulfonylureas are capable of producing severe hypoglycemia. Proper patient selection, dosage, and instructions are important to avoid hypoglycemia. Renal or hepatic insufficiency may increase the risk of hypoglycemic reactions. Elderly, debilitated or malnourished patients and those with adrenal or pituitary insufficiency are particularly susceptible to the hypoglycemic action of glucose-lowering drugs. Hypoglycemia may be difficult to recognize in the elderly or people taking beta-adrenergic blocking drugs. Hypoglycemia is more likely to occur when caloric intake is deficient, after severe or prolonged exercise, when alcohol is ingested, or when more than one glucose-lowering drug is used.

Loss of Control of Blood Glucose: A loss of control may occur in diabetic patients exposed to stress such as fever, trauma, infection or surgery. It may then be necessary to discontinue GLUCOTROL and administer insulin.

Laboratory Tests: Blood and urine glucose should be monitored periodically. Measurement of glycosylated hemoglobin may be useful.

Information for Patients: Patients should be informed of the potential risks and advantages of GLUCOTROL, of alternative modes of therapy, as well as the importance of adhering to dietary instructions, of a regular exercise program, and of regular testing of urine and/or blood glucose. The risks of hypoglycemia, its symptoms and treatment, and conditions that predispose to its development should be explained to patients and responsible family members. Primary and secondary failure should also be explained.

Drug Interactions: The hypoglycemic action of sulfonylureas may be potentiated by certain drugs including nonsteroidal anti-inflammatory agents and other drugs that are highly protein bound, salicylates, sulfonamides, chloramphenicol, probenecid, coumarins, monoamine oxidase inhibitors, and beta adrenergic blocking agents. *In vitro* studies indicate that GLUCOTROL binds differently than tolbutamide and does not interact with salicylate or dicumarol. However, caution must be exercised in extrapolating these findings to a clinical situation. Certain drugs tend to produce hyperglycemia and may lead to loss of control, including the thiazides and other diuretics, corticosteroids, phenothiazines, thyroid products, estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetics, calcium channel blocking drugs, and isoniazid. A potential interaction between oral miconazole and oral hypoglycemic agents leading to severe hypoglycemia has been reported. Whether this interaction also occurs with the intravenous, topical, or vaginal preparations of miconazole is not known.

Carcinogenesis, Mutagenesis, Impairment of Fertility: A 20-month study in rats and an 18-month study in mice at doses up to 75 times the maximum human dose revealed no evidence of drug-related carcinogenicity. Bacterial and *in vivo* mutagenicity tests were uniformly negative. Studies in rats of both sexes at doses up to 75 times the human dose showed no effects on fertility.

Pregnancy: Pregnancy Category C. GLUCOTROL (glipizide) was found to be mildly fetotoxic in rat reproductive studies at all dose levels (5-50 mg/kg). This fetotoxicity has been similarly noted with other sulfonylureas, such as tolbutamide and tolazamide. The effect is perinatal and believed to be directly related to the pharmacologic (hypoglycemic) action of GLUCOTROL. In studies in rats and rabbits no teratogenic effects were found. There are no adequate and well controlled studies in pregnant women. GLUCOTROL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Because recent information suggests that abnormal blood glucose levels during pregnancy are associated with a higher incidence of congenital abnormalities, many experts recommend that insulin be used during pregnancy to maintain blood glucose levels as close to normal as possible.

Nonteratogenic Effects: Prolonged severe hypoglycemia has been reported in neonates born to mothers who were receiving a sulfonylurea drug at the time of delivery. This has been reported more frequently with the use of agents with prolonged half-lives. GLUCOTROL should be discontinued at least one month before the expected delivery date.

Nursing Mothers: Since some sulfonylurea drugs are known to be excreted in human milk, insulin therapy should be considered if nursing is to be continued.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS: In controlled studies, the frequency of serious adverse reactions reported was very low. Of 702 patients, 11.8% reported adverse reactions and in only 1.5% was GLUCOTROL discontinued.

Hypoglycemia: See PRECAUTIONS and OVERDOSAGE sections.

Gastrointestinal: Gastrointestinal disturbances, the most common, were reported with the following approximate incidence: nausea and diarrhea, one in 70; constipation and gastralgia, one in 100. They appear to be dose-related and may disappear on division or reduction of dosage. Cholestatic jaundice may occur rarely with sulfonylureas. GLUCOTROL should be discontinued if this occurs.

Dermatologic: Allergic skin reactions including erythema, morbilliform or maculopapular eruptions, urticaria, pruritus, and eczema have been reported in about one in 70 patients. These may be transient and may disappear despite continued use of GLUCOTROL; if skin reactions persist, the drug should be discontinued. Porphyria cutanea tarda and photosensitivity reactions have been reported with sulfonylureas.

Hematologic: Leukopenia, agranulocytosis, thrombocytopenia, hemolytic anemia, aplastic anemia, and pancytopenia have been reported with sulfonylureas.

Metabolic: Hepatic porphyria and disulfiram-like alcohol reactions have been reported with sulfonylureas. Clinical experience to date has shown that GLUCOTROL has an extremely low incidence of disulfiram-like reactions.

Endocrine Reactions: Cases of hyponatremia and the syndrome of inappropriate antidiuretic hormone (SIADH) secretion have been reported with this and other sulfonylureas.

Miscellaneous: Dizziness, drowsiness, and headache have been reported in about one in fifty patients treated with GLUCOTROL. They are usually transient and seldom require discontinuance of therapy.

OVERDOSAGE: Overdosage of sulfonylureas including GLUCOTROL can produce hypoglycemia. If hypoglycemic coma is diagnosed or suspected, the patient should be given a rapid intravenous injection of concentrated (50%) glucose solution. This should be followed by a continuous infusion of a more dilute (10%) glucose solution at a rate that will maintain the blood glucose at a level above 100 mg/dL. Patients should be closely monitored for a minimum of 24 to 48 hours since hypoglycemia may recur after apparent clinical recovery. Clearance of GLUCOTROL from plasma would be prolonged in persons with liver disease. Because of the extensive protein binding of GLUCOTROL (glipizide), dialysis is unlikely to be of benefit.

DOSAGE AND ADMINISTRATION: There is no fixed dosage regimen for the management of diabetes mellitus with GLUCOTROL; in general, it should be given approximately 30 minutes before a meal to achieve the greatest reduction in postprandial hyperglycemia.

Initial Dose: The recommended starting dose is 5 mg before breakfast. Geriatric patients or those with liver disease may be started on 2.5 mg. Dosage adjustments should ordinarily be in increments of 2.5-5 mg, as determined by blood glucose response. At least several days should elapse between titration steps.

Maximum Dose: The maximum recommended total daily dose is 40 mg.

Maintenance: Some patients may be effectively controlled on a once-a-day regimen, while others show better response with divided dosing. Total daily doses above 15 mg should ordinarily be divided.

HOW SUPPLIED: GLUCOTROL is available as white, dye-free, scored diamond-shaped tablets imprinted as follows: 5 mg tablet—Pfizer 411 (NDC 5 mg 0049-4110-66) Bottles of 100; 10 mg tablet—Pfizer 412 (NDC 10 mg 0049-4120-65) Bottles of 100.

CAUTION: Federal law prohibits dispensing without prescription.

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Recrudescent Pulmonary Melioidosis

A Case Report Involving the So-Called 'Vietnamese Time Bomb'

ROBYN K. GOSHORN, M.D.
Franklin

THOUSANDS OF United States military personnel became infected with *Pseudomonas pseudomallei* while serving in Southeast Asia in the 1960s and 1970s. Serologic surveys have revealed positive titers for this organism in one to seven percent of U.S. soldiers returning from Vietnam.[1,2] Most of these primary infections were asymptomatic.

An important characteristic of this uncommon organism is its ability to produce latent infection which can reactivate many years after primary exposure. Because of the large number of exposed persons and this propensity for late reactivation, melioidosis has been called the "Vietnamese time bomb,"[3] and warnings were issued to clinicians during the 1960s and 1970s to be alert for this disease.[4,5] Nevertheless, reports of recrudescent melioidosis have not been commonplace.

Report of a Case

A 35-year-old white man was brought to the hospital complaining of cough, fever and dyspnea. He had become ill about one week before admission with fever in the range of 101 degrees Fahrenheit, sweats, wheezing, and a cough productive of yellow, blood-tinged sputum. Therapy prior to admission had consisted of six days of erythromycin and three days of doxycycline without improvement in symptoms. His wife and son had had symptoms compatible with viral respiratory infection several days prior to the onset of the patient's illness. In 1970 he served with the Special Forces in Vietnam. He had a history of asthma since childhood and during the 1970s required multiple hospitalizations for control of bronchospasm. For eight years before admission he had taken Prednisone, 5 mg. three times a day.

His physical examination on admission revealed a temperature of 97.6 degrees Fahrenheit, blood pressure 152/100, and pulse 88. He had a paroxysmal cough but otherwise did not appear seriously ill. His chest examination was unremarkable as was the rest of his physical examination.

The chest x-ray revealed nodular infiltrates in the right mid and upper lung field (*Figure*). The white blood cell count was 12,200, with 77% neutrophils and 23% lymphocytes. A gram stain of his sputum revealed many neutrophils and small numbers of gram-positive cocci and gram-negative rods.

He was treated with intravenous chloramphenicol 50 mg. per kg. per 24 hours, and oral tetracycline hydrochloride 2 gm. per 24 hours. Five days after starting therapy, his infiltrates had cleared completely.

A culture of expectorated sputum grew "normal flora," and cultures of the blood were sterile. The sputum was negative for eosinophils, acid-fast bacilli and fungal organisms. A sputum fluorescent antigen study for influenza type B was negative. An influenza type A fluorescent antigen study was not completed for technical reasons. Indirect hemagglutination titers for *Pseudomonas pseudomallei* were performed by the Center for Disease Control in Atlanta and found to be positive at 1 to 40 on the day of admission and 1 to 80 two weeks later.

Clinical clues that led to the diagnosis of melioidosis in this patient were his history of travel to an endemic area and the nodular appearance of his pulmonary infiltrate. His positive hemagglutionation titer and prompt response to therapy confirmed the diagnosis despite inability to culture the organism.

Pseudomonas pseudomallei is an aerobic, motile, non-encapsulated, bipolar staining gram-negative rod, which may resemble a closed safety pin in gram stain.[2] It was first described in 1912 by Whitmore and Krishnaswami and named bacillus pseudomallei because of its resemblance to bacillus mallei, the etiologic agent of the equine disease glanders.

Pseudomonas pseudomallei can be grown on standard solid and broth media. Typical wrinkled colonies take at least 72 hours to develop, and it has been recommended that plates be observed for at least a week.[6] In a series of 39 patients with proven pulmonary melioidosis, it was possible to culture the organism from expectorated sputum in only 28 (74%).[1]

The endemic area for melioidosis is limited to a band 20 degrees north and 20 degrees south of the equator.[6] In addition to the major focus in Southeast Asia, endemic cases have been reported from Asia Minor, Madagascar, Guam and Australia. Sporadic cases have occurred in Korea, the

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Philippines, Equador, Panama and Russia.[2]

Pseudomonas pseudomallei is ubiquitous in soil and water in Vietnam.[7] Infection can be acquired by inhalation of contaminated dust or aerosol or by percutaneous inoculation of broken skin. Rare instances of transmission by intravenous inoculation in drug addicts,[6] venereal transmission,[6] and acquisition of the infection by laboratory personnel[8] have been reported.

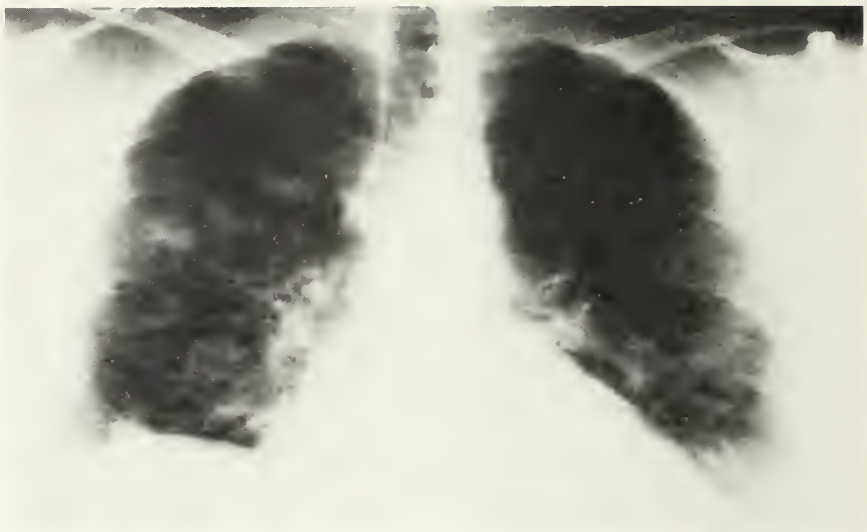
Melioidosis is a very common infection in the native populations of endemic areas. Serologic evidence of exposure has been found in 29% of persons in Thailand,[2] 16% of persons in Malasia,[2] and 7% to 10% of adult males throughout the Malay Peninsula.[9]

Pseudomonas pseudomallei may cause gram-negative septicemia with a fatality rate of at least 30%, even with appropriate antibiotic therapy.[6] It may also produce indolent infection with abscesses and sometimes sinus tracts in viscera, skin, bone and lymph nodes. The organ most commonly affected, however, is the lung.

The radiographic appearance of pulmonary melioidosis[1,2] is characterized by nodular infiltrates with a predilection for upper lobes often associated with cavitation. Cavities are usually thin-walled and single. Hilar adenopathy and pleural effusion rarely are seen. The similarity of the radiographic appearance of pulmonary melioidosis to that of pulmonary tuberculosis has been emphasized.[9]

Pulmonary melioidosis may present as an acute illness with fever, chills, pleuritic chest pain, and cough productive of purulent or bloody sputum.[1,9] Advanced cavitary disease may also present as an incidental finding on routine chest x-ray in an asymptomatic person.[9] Weight loss is a common sign.[1,9] Leukocytosis is usually mild (mean WBC 12,000), and neutrophilia is absent or mild.[1,9] There are no other characteristic laboratory or physical findings.

In addition to these well recognized clinical patterns, a number of unusual manifestations of melioidosis have been reported[2] including endo-, myo-, and peri-carditis, cholecystitis, ulcerative colitis, urinary tract infection, puerperal sepsis, septic arthritis, and parotitis.[6]



Chest x-ray reveals nodular infiltrates in the right mid and upper lung field.

Recrudescent disease can take on any of the patterns described above,[4,6] and reactivation has been reported as long as 24 years after primary exposure.[6] Events reported to precipitate reactivation of disease include trauma, burns, diabetic ketoacidosis, surgical procedures, and steroid therapy.[6,7] Reactivation has also followed acute infection with other organisms, including influenza A, *Streptococcus pneumoniae*, and plasmodium.[5,6,7] The biologic phenomena involved in latency and recrudescence of this organism are not fully understood.[4]

The organism is generally susceptible to tetracycline, chloramphenicol, and sulfonamides at the concentrations achievable with conventional doses.[2] Synergy has been demonstrated between tetracycline and chloramphenicol and between trimethoprim and sulfamethoxazole.[6] Antibiotic antagonism has been demonstrated with multi-drug regimens including trimethoprim-sulfamethoxazole, tetracycline, chloramphenicol and kanamycin.[10] The optimal duration of therapy is not certain, but is relatively long. In treating pulmonary melioidosis, Everett and Nelson found invariable relapse with treatment courses of 14 days.[1] The mean duration of successful therapy in their series of 38 patients was 60 days, with a range of 30 to 150 days. Surgical removal of cavitary disease was often necessary to achieve bacteriologic cure.

Summary

The spectrum of pulmonary and extra-pulmonary disease caused by *Pseudomonas pseudomallei* is broad, and this organism can cause acute infection after latent periods lasting many years. History of travel to an endemic area is a major clinical clue to early diagnosis, which is important since the organism is usually susceptible to appropriate antimicrobial therapy.

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Reader Comments on CME Article, 'Carcinoma of the Prostate'

Letter to the Editor

Re the CME article, "Carcinoma of the Prostate: Is Radiation Therapy an Alternative to Radical Prostatectomy?" by James G. Morphis II, M.D., and Ned B. Hornback, M.D. (INDIANA MEDICINE, December 1986).

The authors use two graphs derived from well known series to support the statement that "resectable carcinoma (below stage C) will tend to demonstrate a five- and ten-year survival similar to age-adjusted expected survival of the general population whether treated by radical surgery or irradiation." Alas, neither graph includes the vital control series of patients with negative nodes who received no treatment at all.

Such a control series would be impossible in our litigious society. Nevertheless, the high incidence of histologic carcinoma of the prostate in men over 50 in autopsy series of accidental deaths allows *inference* that the decay curve of a prospectively randomized group of *untreated* node-negative men might be similar to those depicted in the article.

Because our lawyers have nearly destroyed the possibility of randomized clinical trials in this country, inference has to be permitted. Why do we Americans require a college degree prior to the M.D. if not to develop skill at inference? In my opinion, it is, if from a competitive department within a tough school, a license that protects, to some extent, the public against woozy, metaphysical, romantic, 19th century speculation.[1]

I used to be impatient with articles that did not at least mention the absence of randomized controls in the discussion section until I learned that "the first published modern randomized clinical trial, reported in 1948, was that of Daniels and Hill, which showed streptomycin to be highly efficacious in treating tuberculosis."[2,3,4]

1948 is not so long ago. I suppose our culture might be forgiven for being slow to assimilate a disembodied technology like randomization. After all, it took the British Navy 48 years to issue lemons to its sailors, even though they commissioned the original controlled (but not randomized) experiment.[2] On the other hand, time may be running short; the Supreme Court has ruled that vaginal jelly caused a malformation, pure poppycock in terms of science, of grave import for our people. If professional scientists are fuzzy about causation, we cannot expect the courts to do much better. — **Anthony H. Horan, M.D., South Bend, Ind.**

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The Author Replies

I have appreciated Dr. Horan's comments regarding the recognized need for randomized controls in scientific endeavors. The inference, from the incidence of occult cancer in autopsy series, that the survival of a control group of patients with node-negative primary untreated disease might approximate that of the patients receiving conventional therapy is, however, best left untested.

As practitioners of the art and science of medicine, we have dual obligations: 1) That of providing the maximal benefit to our patients on the basis of current technology, and 2) that of continually improving our understanding and treatment of disease. The latter is, of course, best served by randomized clinical trials.

Pursuit of the question, however, of the natural history of node-negative primary untreated disease should not supersede our responsibility to the patient. By withholding currently accepted local treatment for clinically evident disease of the prostate, the patient is needlessly subjected to the risks, not only of possible subsequent metastases, but also the morbidity of urinary obstruction. — **James G. Morphis II, M.D., Indianapolis**

The Impact on Public Health of Routine HTLV-III Antibody Testing

A National Institutes of Health Consensus Report Synopsis

THE APPEARANCE OF acquired immune deficiency syndrome (AIDS) has brought suffering and death to those who are afflicted and, at the same time, has posed daunting challenges to those who care for the sufferers, to biomedical scientists, and to those responsible for public health and public policy. Among these challenges is the protection of the nation's blood supply from contamination by human immunodeficiency virus (HIV),* the causative agent of AIDS.

This challenge was met rapidly by the development of laboratory tests to detect the presence of antibody against the virus. The application of these tests makes it possible to determine whether the person has been infected by the virus at some time and thus to exclude persons from donating blood or to discard blood already donated. In the past 15 months, the widespread application of these tests along with self-deferral and removal of HIV-positive subjects from the pool of donors has sharply reduced the likelihood of the virus being spread by way of blood products.

*Previously referred to as HTLV-III/LAV, and subsequently referred to in this document as HIV in accordance with emerging and recommended usage.

This synopsis is based on an NIH consensus development conference conducted in 1986. The complete consensus statement is available free of charge from the Office of Medical Applications of Research, National Institutes of Health, Bldg. 1, Rm. 216, Bethesda, Md. 20892.

Remarkable progress has recently been made in isolating the virus and in developing reasonably reliable tests for detecting its presence in blood by measuring the formation of antibodies against it. Mobilization of the whole scientific community, from government agencies and industry to the individual investigator, has brought about this progress, boding well for the eventual prevention of the disease. In fact, the prevention of posttransfusion AIDS is a typical example of the gains to be achieved by many years of supporting basic research.

However, the introduction of these tests has brought with it some problems. Questions can be raised about interpretation of the tests and their extension to purposes other than protection of the blood supply. As with almost every aspect of AIDS, the facts, opinions, and uncertainties of science are rapidly translated into public beliefs and social policy. Often, this translation has been inaccurate and incorrect. Policy has been made, or recommended, on the basis of an assumed scientific certitude that in fact may not exist. Conversely, scientifically sound information has been ignored or distorted by policymakers. Scientists have often failed to communicate their findings in ways that are useful for public policy.

The tests for evidence of infected blood are not yet optimally effective. There is still room for improved applications of the scientific method to identify methods with increased sensitivity, specificity, and predictive value. Because no test can be totally devoid of error, there must be continuing vigorous efforts to educate the public about who is a suitable donor of blood and to facilitate anonymous self-deferral at the time of blood donation.

To enhance understanding among scientists, those responsible for the health of individuals and of society, and the public at large, the National Heart, Lung, and Blood Institute of the National Institutes of Health (NIH) and the NIH Office of Medical Applications of Research sponsored this Consensus Development Conference on the Impact of Routine HIV-Antibody Testing of Blood and Plasma Donors on Public Health. Other sponsors of the conference were the Centers for Disease Control; the Food and Drug Administration; the Clinical Center, NIH; the National Institute of Allergy and Infectious Diseases, NIH; and the National Institute of Mental Health.

The conference brought together biomedical investigators, blood bank specialists, clinicians, consumers, and representatives of public interest groups. Following two days of presentations by medical experts and discussion by the audience, the consensus panel worked hard to interpret the scientific evidence. Comments and recommendations are organized according to the following questions:

1. What tests are currently being used? What are their performance characteristics?

There are three approaches to detecting HIV infection. Listed in decreasing order of difficulty and expense, these are:

1. Detection of the virus by culturing it.
2. Detection of antigens elaborated by the virus and present in blood.
3. Detection of HIV-specific antibodies that are produced by the infected person's immune system.

Two tests mainly support the entire current testing program. Both are of the third type. ELISA (enzyme-linked immunosorbent assay) reacts to the presence of antibodies in the donor's blood, showing a more intense color as larger quantities of the antibodies are present in the serum. A positive reaction is recorded where the observed intensity exceeds a cutoff value set by the manufacturer of the test kit. If the cutoff value is set low, so that relatively faint specimens are recorded as positive, the chance of detecting HIV cases with low levels of antibody are increased. At the same time, such a low threshold increases the chance of recording as positive samples that do not contain antibodies against HIV which can also produce color in the system. To protect the blood supply, it is prudent for a given test to set the threshold low, and accept the increase in false positives that must accompany that low threshold.

With a low threshold the ELISA test is quite sensitive; that is, truly infected persons are highly likely to give a positive reaction. But, uninfected persons—who are vastly more numerous—also occasionally give positive reactions to this test. This small fraction of uninfected donors produces many more of the positive reactions than arise from positive reactions of the few persons actually HIV-infected. That is, the odds are great that any single ELISA-positive reading comes from an uninfected person. Furthermore, low positive values are often not reproducible; that is, a repeated, independent sample from a donor whose first test was barely positive will likely turn up negative.

Current practice is that all donors are ELISA-tested. If the test is negative the unit of blood is acceptable. If there is a positive reaction, two further ELISA tests are performed on the same unit. If both are negative, the unit is acceptable. If either is positive, the unit is classified as "repeatedly reactive" and is destroyed.

In the nonprofit blood banking system, there is further testing of the blood of a repeat reactor, aimed at clarifying the person's HIV status, which is still ambiguous since so many HIV false positives occur among the ELISA repeat reactors. The Western blot test is then applied. It, too, is an antibody detecting test, but it differs from the ELISA in several ways:

1. It gives information about particular antibodies among the several that HIV antigens may elicit; prominent among these are antibodies against p24 and gp41.
2. It uses electrophoresis and is thus more expensive and demanding of expertise than the ELISA.
3. It is less likely to give a false positive or false negative result.

If the specimen is Western-blot-positive, the donor is regarded as infected with HIV and notification of the donor is attempted. If the repeat reactor's Western blot test is negative, the donor may be informed that:

1. The blood is not, and will not be, usable.
2. The donor in all probability is not infected.

To protect the quality of the blood supply, it is essential to reduce the number of false negatives to a minimum. However, false negatives cannot be totally eliminated because some sera contain too little anti-HIV antibody to be detected; they come primarily from donors who have been infected very recently, typically during the first 6 weeks of infection, or from individuals who for one reason or another form antibody very slowly. It is essential to increase the sensitivity of methods for detecting anti-HIV-antibody and to develop methods to detect and measure HIV antigens or infected T_4 cells.

Reasonably Reliable Tests Now Exist to Detect the AIDS Virus in Blood

Several versions of the ELISA test are on the market. They differ in their comparative sensitivity to the various antigens of HIV, and thus reflect somewhat different information about the antibodies in a given blood sample. They also presumably differ in sensitivity to sample constituents responsible for false positives. The cost-benefit ratio of simultaneously using ELISA tests from two different manufacturers on each sample to improve accuracy should be explored.

Several other methods of detecting anti-HIV antibodies are very useful for confirming and extending results obtained by the ELISA method, but are more time-consuming. Western blotting is difficult to standardize, but staining of p24 together with gp41 is unequivocally positive. Correlation with intermediate and high ELISA values is excellent. Radioimmune precipitation (RIP) and radioimmune assay (RIA) can be made both sensitive and specific by using very highly labeled antigens, but require skilled personnel and involve the use of radioactivity. HIV isolation is very difficult, time-consuming, and requires highly skilled personnel; it does not lend itself to analysis of large numbers of samples. It correlates highly with high ELISA

values.

The most promising new approaches will be the development of fluorescent antibody (FA) techniques for detecting infected T_4 lymphocytes and the development of techniques for detecting viral proteins, based either on antigen capture or on reverse transcriptase (RT) activation and synthesis of HIV DNA, which can then be detected with high sensitivity and specificity.

2. What constitutes a positive test? How should a positive HIV-antibody test result be interpreted? How should these tests be used?

The virus thought to cause AIDS has been isolated and its genome and gene products are largely characterized. Tests have been developed for the detection of virus, virus-coded proteins, and antibodies directed against those proteins. These developments have facilitated large-scale screening of blood and blood products for viral antibodies. Clearly, the tests in use have enhanced the safety of transfusion procedures.

Clearly, the Tests in Use Have Enhanced the Safety of Transfusion Procedures

Current procedures utilize an ELISA test for detecting antibodies against HIV as an initial screen. An additional test, the Western blot, is used to test sera found repeatedly reactive in the ELISA test. Extensive experience has demonstrated that many sera that are reportedly reactive in the ELISA test do not react when tested by Western blot analysis. These discordant results indicate that many of the sera that are repeatedly reactive in the ELISA test do not represent combinations with virus-specific proteins and often may not indicate the presence of an HIV infection.

Resolution of this problem is difficult because of limitations in currently available information. This is partly because investigators often use different methodologies, and licensed tests from different manufacturers probably differ in subtle yet possibly important ways. There are few published comparative analyses of the tests used in the field. Further, Western blots have generally been carried out by personnel who are aware of the fact that the sera they are testing have reacted in the ELISA test. In addition, it often is not possible to estimate the specificity of these tests because ELISA-negative sera are not being routinely tested by Western blot. Consequently, there is still a need for rigorous studies to clarify many issues regarding interpretation of test results.

The most specific test for infectivity remains virus isolation; however, because of the complexity and difficulty of isolating HIV in cell culture, this is an impractical method for large-scale use. Some form of the ELISA test with enhanced sensitivity and specificity remains the most practical and feasible procedure for large-scale screening of the blood supply. Improved confirmatory methods should be developed that can be used in conjunction with such a test. Even with currently available tests, however, it is essential that confirmatory studies be performed without the laboratory personnel knowing the prior ELISA results. Specimens should be identified by a code number only and a suitable number of ELISA-negative specimens should be included in each test run.

For the purposes of notifying the donor, a confirmatory test such as the Western blot should be applied to resolve the actual HIV status because the repeated reaction may be caused by factors such as autoimmune or cell-line-specific antibodies. Currently, however, blood banks are obliged to exclude sera that test repeatedly reactive in the ELISA regardless of any confirmatory test results. Many of these almost certainly represent false positive reactions. It is unfortunate that a considerable number of donors are functionally excluded from donation because of their questionable test status. Efforts should therefore be made to find ways to identify ELISA-positive individuals who are not infected so that their true serological status may be defined and their return to the blood donor pool expedited.

Available data indicate that the presence of virus precursors or antibodies in the blood reflects the continuing presence of HIV in the host. Thus, detection of such components represents a sign of continued infectivity of the blood. Like many other chronic viral infections, the period very shortly after exposure is often likely to be characterized by lack of antibody and by levels of virus proteins below the threshold of detection. In addition, biologic variation of both host and pathogen suggest that some chronically infected individuals do not synthesize virus-specific antibodies or make quantities of viral proteins that can be detected by assays currently in use. Nevertheless, such individuals are potentially infectious. Thus, while total elimination of infected blood from the national supply is not immediately feasible, it remains a desirable goal.

3. How should positive test results be handled?

A positive test* has the following significance as currently understood:

*Positive: describes a repeatedly reactive sample which is determined to contain antibody by an additional, more specific test, such as Western blot, radioimmunoprecipitation, and the like. Persons who have positive sera are termed "seropositive."

1. Such persons are infected with HIV.

2. Most persons infected with retroviruses such as HIV are infected for life.

3. All persons who are antibody-positive for HIV, whether they are symptom-free or ill, must be considered to be potentially infectious to others by sexual transmission, by sharing of drug injection equipment, by childbearing, or by donation of blood, semen, or organs.

4. Antibody positivity is not synonymous with having AIDS. However, by current estimate, as many as 35 percent of HIV-antibody-positive persons may experience progression to AIDS over 6 to 8 years.

5. We cannot precisely predict who among persons with antibody positivity will be ill or fatally ill in the future and it is not possible at present to prevent such outcomes.

6. All antibody-positive persons should seek information and advice on how to protect their sexual contacts and future children from infection.

The panel believes that there is a clear ethical responsibility on the part of blood- and plasma-collection centers to notify individuals with repeatably reactive blood in a sensitive, humane, and supportive manner. Consideration should be given to the donor's cultural and linguistic background. The need to maintain confidentiality of the information creates a duty on the part of blood-collection centers to assume primary responsibility for notifying positive donors of their test results.

Differences exist across communities with respect to the process by which notification is accomplished, the nature of the information provided, and the extent of counseling that is provided. The panel does not believe that any single approach would be universally applicable.

Notification should be followed by education. The panel believes that the central component to education is person-to-person interchange between the donor and the counselor. Additional techniques such as videotape presentations and printed materials may supplement, but not substitute for, personal interchange. Appropriate elements of a supportive counseling program for persons who are seropositive include education about the natural history of HIV infection and the meaning of a positive test, advice on behavioral changes that will protect one's sexual partner(s) from infection, and referral to additional resources.

While blood collection centers will rarely have the trained personnel or assets to provide extensive and specialized counsel, we believe that they have a duty to cooperate with community agencies that can provide the necessary supportive services and to make effective referrals. These referrals would include the person's physician and other long-term counseling services, and such community agencies as local health departments, alternate test sites, AIDS service organizations, and social services agencies.

Confidentiality should be carefully and strictly maintained due to the sensitive nature of the information. Test results should be released to parties other than the patient only when there is a scientifically valid and legitimate need to know for public health purposes and, in principle, with the patient's specific consent.

Current practice in many centers is to enter the names of persons whose blood is repeatably reactive but negative by Western blot into lists of deferred donors. We believe that it is inappropriate to enter a person's identity into such a list without his knowledge and without giving him the personal advantage of sharing that knowledge and its meaning. It is common practice to allow such individuals to donate again, but to discard their blood without their knowledge. This practice should not continue; these donors have a right to be advised of their status.

Blood-collection agencies currently maintain lists of deferred donors onto which are entered the names of HIV-antibody-positive donors. The agencies believe that such lists increase the likelihood that infectious units of blood will be screened out in the future should positive donors not self-defer. On the other hand, such lists are a potential source of loss of confidentiality for donors should their identity be inadvertently revealed. We believe that a balance of interests supports the entry of the names of those who are believed to be truly positive or whose status cannot be satisfactorily resolved but only if such donors are informed initially that their name will be listed, if the list is very securely held, and the list is used only for the limited purpose of protecting the quality of the blood supply. The actual utility of such lists should be regularly evaluated as technology improves.

Persons found to be seropositive may have a history of previous blood donations. For such persons, the question then arises about their past donations that have already been transfused into patients. In these cases, the blood bank has a serious responsibility to notify the hospital to which that blood was sent. It is the responsibility of the hospital, directly or through the patient's physician, to notify the patients of the possibility of having received seropositive blood and to educate them about the meaning of this. It is our opinion that, while the blood banks do not have the primary responsibility for the notification and counseling of recipients, they should, within their means, assist hospitals and physicians with accurate and effective information.

The repeatably reactive donors (by ELISA) in the plasmapheresis setting cannot be characterized without additional testing as being either positive or negative for anti-HIV-antibody. If the plasmapheresis industry is unwilling to test these donors further, the situation should be explained to the donor and the donor should be referred to an agency where such testing and pretest and posttest counseling are available.



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Give your angina patients what they're missing...



CARDIZEM®: FEW SIDE EFFECTS

diltiazem HCl/Marion

- ***Antianginal action includes dilatation of coronary arteries, a decrease in vascular resistance/afterload, and a reduction in heart rate***
- ***Proven efficacy when used alone in angina[1]***
- ***Compatible with other antianginals[2,3*]***
- ***A safe choice for angina patients with coexisting hypertension, asthma, COPD, or PVD[4,5]***

***See Warnings and Precautions.**

Please see brief summary of prescribing information on the next page.



CARDIZEM® diltiazem HCl/Marion

FEW SIDE EFFECTS IN ANTIANGINAL THERAPY

60 mg tid or qid

Brief Summary
Professional Use Information

CARDIZEM®
(diltiazem HCl) 30 mg and 60 mg Tablets

CONTRAINDICATIONS
CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, and (3) patients with hypotension (less than 90 mm Hg systolic).

WARNINGS

1. ***Cardiac Conduction.*** *CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (six of 1,243 patients for 0.48%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of diltiazem.*
2. ***Congestive Heart Failure.*** *Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt).*
   Experience with the use of CARDIZEM alone or in combination with beta-blockers in patients with impaired ventricular function is very limited. Caution should be exercised when using the drug in such patients.
3. ***Hypotension.*** *Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.*
4. ***Acute Hepatic Injury.*** *In rare instances, significant elevations in enzymes such as alkaline phosphatase, CPK, LDH, SGOT, SGPT, and other symptoms consistent with acute hepatic injury have been noted. These reactions have been reversible upon discontinuation of drug therapy. The relationship to CARDIZEM is uncertain in most cases, but probable in some. (See PRECAUTIONS.)*

PRECAUTIONS
General. *CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any new drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses at 20 mg/kg were also associated with hepatic changes, however, these changes were reversible with continued dosing.*

Drug Interaction. *Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS.)*

Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers or digitalis is usually well tolerated. Available data are not sufficient, however, to predict the effects of concomitant treatment, particularly in patients with left ventricular dysfunction or cardiac conduction abnormalities. In healthy volunteers, diltiazem has been shown to increase serum digoxin levels up to 20%.

Carcinogenesis, Mutagenesis, Impairment of Fertility. *A 24-month study in rats and a 21-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response in in vitro bacterial tests. No intrinsic effect on fertility was observed in rats.*

Pregnancy. *Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/posthatal studies, there was some reduction in early individual pup weights and survival rates. There was an increased incidence of stillbirths at doses of 20 times the human dose or greater.*

There are no well-controlled studies in pregnant women; therefore, use CARDIZEM in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. *Diltiazem is excreted in human milk. One report suggests that concentrations in breast milk may approximate serum levels. If use of CARDIZEM is deemed essential, an alternative method of infant feeding should be instituted.*

Pediatric Use. *Safety and effectiveness in children have not been established.*

ADVERSE REACTIONS
Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded.

In domestic placebo-controlled trials, the incidence of adverse reactions reported during CARDIZEM therapy was not greater than that reported during placebo therapy.

The following represent occurrences observed in clinical studies which can be at least reasonably associated with the pharmacology of calcium influx inhibitors. In many cases, the relationship to CARDIZEM has not been established. The most common occurrences as well as their frequency of presentation are: edema (2.4%), headache (2.1%), nausea (1.9%), dizziness (1.5%), rash (1.3%), asthenia (1.2%). In addition, the following events were reported infrequently (less than 1%):

Cardiovascular:	*Angina, arrhythmia, AV block (first degree), AV block (second or third degree — see conduction warnings), bradycardia, congestive heart failure, flushing, hypotension, palpitations, syncope*
Nervous System:	*Amnesia, gait abnormality, hallucinations, insomnia, nervousness, paresthesia, personality change, somnolence, tinnitus, tremor.*
Gastrointestinal:	*Anorexia, constipation, diarrhea, dysgeusia, dyspepsia, mild elevations of alkaline phosphatase, SGOT, SGPT, and LDH (see hepatic warnings), vomiting, weight increase*
Dermatologic:	*Petechiae, pruritus, photosensitivity, urticaria.*
Other:	*Amblyopia, dyspnea, epistaxis, eye irritation, hyperglycemia, nasal congestion, nocturia, osteoarthritic pain, polyuria, sexual difficulties.*

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: alopecia, gingival hyperplasia, erythema multiforme, and leukopenia. However, a definitive cause and effect between these events and CARDIZEM therapy is yet to be established.

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See complete Professional Use Information before prescribing.

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HYPERBARIC MEDICINE

A Specialized Mode of Treatment That Is Gaining Acceptance

MARK HARRIS, M.D.[1]
DEBRA YOUNG, M.D.[2]
Evansville

HYPERBARIC MEDICINE, which has long been a military science, is fast becoming an accepted form of therapy for many types of emergent and non-emergent civilian disorders. This multi-faceted form of therapy is gaining acceptance and status in the medical community for treatment of a variety of maladies such as carbon monoxide poisoning, arterial gas embolism, and enhancement of problem wound healing, to mention only a few.

Recent research has expanded the scope of hyperbaric oxygen therapy, and along with more economically feasible chamber designs, the number of active hyperbaric chambers in the United States has greatly increased in the past seven years. A recent survey shows that in 1979 there were 57 operating chambers in the U.S. Since then, the number of active chambers has increased by approximately 60 new units per year.[1]

Unfortunately, this sudden onslaught of "new wave" HBO medicine has created a simultaneous knowledge deficit, primarily because this specialized area of treatment is not usually included in present medical school curricula. Consequently, the purpose of this article is to impart knowledge of basic baromedical physiology, and to outline current rationale for the use of high pressure oxygen in accepted treatment practices for specific individual disorders.

Definition of HBO

The Undersea Medical Society's publication, "Hyperbaric Oxygen Therapy: A Committee Report," defines hyperbaric oxygenation as: "A mode of medical treatment in which the patient is entirely enclosed in a pressure chamber breathing oxygen at a pressure greater than one atmosphere. Breathing 100% oxygen at one atmosphere pressure or applying oxygen topically to parts of the body without the use of a pressurized chamber which encloses the patient completely is not considered hyperbaric oxygenation."[2]

Chamber Design

Two types of hyperbaric chambers exist: monoplace and multiplace chambers.[3] A *monoplace* hyperbaric chamber (*see Fig. 1*) is a three atmosphere, semi-portable, cylindrical, usually acrylic unit. It is pressurized with 100% oxygen via direct wall connection to existing hospital oxygen sources operating at 50-75 psig pressure. The patient lies alone in the chamber, but specialized electronics and mechanical attachments allow for two-way communication, IVs, hemodynamic monitoring, EKG monitoring, pressure-cycled ventilator support, and luxuries such as TV, VCR, and stereo cassette capabilities.[4]

Monoplace chambers are easily operated and require no additional technical staff other than critical care nurses and respiratory therapists who are specially trained in monoplace baromedicine. Because of increasing capabilities, low cost, minimal technical support, and low maintenance, these units are now the most plentiful chambers in the country today.

Multiplace chambers are large multiroom treatment facilities which are of six atmosphere design. They are compressed with air (instead of oxygen like the monoplace chambers) and oxygen is delivered at elevated pressures to the patients via several mechanisms including aviator masks, hoods, or ventilators. They have "medical locks" allowing personnel and equipment in and out of the chamber during treatments. Usually these chambers can treat more than one person at a time and there is the luxury of "hands on" capability with any critical care patient during treatment.[5]

Even though these chambers are the state of the art in design, huge costs are incurred for required hardware (compressors, chamber, plumbing), technical support (certified chamber operators), and operating expenses. Thus, these chambers are found at very few civilian medical institutions.

Gas Laws

Before beginning an intelligent discussion of the clinical effects of HBO, a brief review and understanding of the basic gas laws involved in baromedicine is in order. Much of HBO theory can best be understood by reviewing Henry's Law. Simply stated, Henry's Law decrees that the amount of gas dissolved in a solution is proportional to the partial pressure of that

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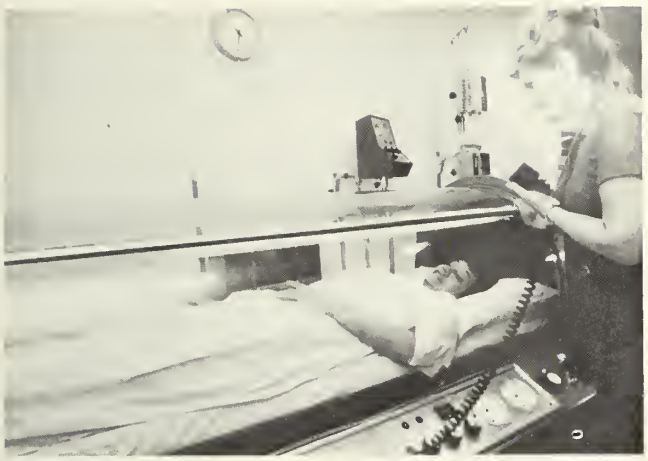


FIGURE 1: The Sechrist Monoplace Hyperbaric Chamber in use at Deaconess Hospital, Evansville.



FIGURE 2: A diabetic foot ulcer that had not responded to conventional therapy.



FIGURE 3: The foot ulcer (same patient as shown in Figure 2) after 22 hyperbaric oxygen treatments. Note the granulation tissue at wound periphery.

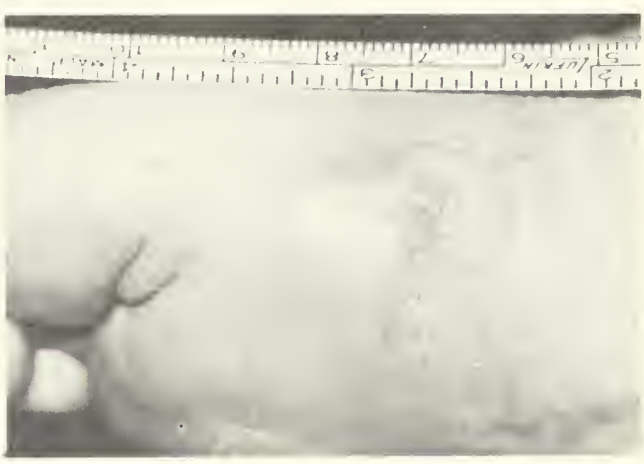


FIGURE 4: The healed foot ulcer (same patient as shown in Figures 2 and 3) indicates the result of 60 hyperbaric oxygen treatments over an approximately three-month period.

gas exerted on that solution and the solubility of that gas in that solution. Using a chamber to create several atmospheres of pressure of oxygen causes extremely high levels of oxygen to be dissolved into the plasma via the pulmonary alveolar tree. It is this oxygen enriched plasma that induces most of the clinical effects seen in HBO.

One other gas law paramount to the discussion of HBO is Boyle's Law, which states that as the pressure increases, the volume of any gas under such pressure decreases. The effects of Boyle's Law aid the treatment of arterial gas embolism and decompression sickness, wherein the high chamber pressures diminish the bubble size of intravascular air, thus relieving some of the vascular obstruction encountered in these clinical maladies.[6]

Clinical Effects of HBO

A synopsis review of the clinical effects of HBO reveals three major areas of concern: HBO and wound healing; HBO and smoke inhalation; and HBO use in intravascular bubble formation.

HBO promotes wound healing in ischemic wounds by enhancing wound antisepsis, stimulating neovascularization of the wound, and stimulating collagen production (*see Fig. 2*). Wound antisepsis is enhanced by supplying oxygen to a NADPH-oxidase enzyme within the leukocyte's phagocytic vacuole which produces free oxygen radicals to catabolize invading organisms.[7] HBO also stops gas gangrene progression by inhibiting alpha toxin production, a c-lecinthinase produced by clostridial organisms and the main toxin responsible for the severity of gas gangrene.[8]

In addition to antisepsis, HBO stimu-

lates angiogenesis in poorly healing ischemic wounds.[9,10,11] Certain wounds heal poorly secondary to chronic local tissue hypoxia induced by either local microvasculature angiopathy (such as in diabetes, vasculitis, steroid treated patients, or radiation induced obliterative endarteritis) or more generalized disease states (such as proximal arteriosclerosis or chronic stasis edema). The bottom line is that low periwound oxygen tensions inhibits granulation tissue formation, and without the development of this neovascular bed, subsequent wound healing will not occur.

HBO has been shown to elevate local tissue oxygen tensions in ischemic wounds by enhancing the diffusion gradient from the plasma to the wound. This enhancement of the local periwound oxygen tensions leads to an increase in angiogenesis and thus granulation tissue formation, (*Fig. 3*) ultimately setting in motion the proper wound healing sequence. The exact physiological mechanism by which HBO induces angiogenesis in such wounds is not well understood, but is probably related to the neovascular phenomena seen in retrolental fibroplasia, an effect of oxygen on premature blood vessels (*Fig. 4*).

Besides the above effects, HBO is vital to the healing process of ischemic wounds because oxygen is necessary for hydroxylation of proline and lysine via prolyl-lysyl hydroxylase (Km for oxygen is 20-30 mm Hg).[12,13] This step is key to the formation of mature collagen from the single stranded variety, and a step which is impeded in wounds with low periwound oxygen tensions (such as wounds described in the preceding paragraph).

In smoke inhalation, the elevated plasma concentration of oxygen provided by HBO competes for carbon monoxide (CO) and cyanide (CN) at the blood and tissue level, reducing the toxic effects of the poisons. CO and CN bind readily to hemaglobin and many intracellular components, including cytochrome a^3 oxidase of the electron transport chain, to effect global tissue ischemia. HBO reduces the elimination T1/2 for tissue bound CO and CN, promoting survival of neurons and this hopefully diminishing certain long-term neurologic sequelae associated with CO and CN poisonings.[14-16]

Intravascular bubbles emanate from both arterial gas embolism and decompression sickness (the "Bends"). In many clinical situations air bubbles can enter the arterial tree and therefore into the brain causing sudden severe stroke syndromes. Some such situations include art lines, posterior fossa surgery, dialysis, cardiovascular surgery, and air via intravenous lines through a patent foramen ovale. Air bubbles can also form intravascularly in decompression sickness from too rapid depressurization of a person breathing compressed air. Hyperbaric oxygen therapy is helpful in reducing the size of intravascular bubbles via direct pressure effect in accordance with Boyle's Law, and by eluding off the relatively insoluble nitrogen from within the bubble and its replacement with very soluble oxygen (in accordance to Henry's law).[17-21]

Summary

It is not possible to cover the comprehensive field of HBO medicine in one short review. The goal here was to review basic baromedical principles, and thus lay a foundation of medical knowledge for the practicing physician who may not have been exposed to HBO medicine during formal medical training.

HBO is helpful in wound healing because it enhances wound antisepsis, collagen production, and wound angiogenesis. Furthermore, HBO helps in toxic disorders such as CO and CN poisonings by enhancing removal of the deleterious gases from the tissues. Finally, HBO enhances resolution of intravascular bubbles formed by whatever mechanism.

In Indiana, hyperbaric chambers are found in Indianapolis and Evansville. A complete listing of hyperbaric chambers can be obtained from the Undersea Medical Society at Bethesda, Maryland.

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1986 MEMBERSHIP REPORT
December 31, 1986

County	Active	1st Year	Resident	Senior	Inactive	Hardship	Totals
Adams	11	1		3			15
Bartholomew-Brown	71		1	8	5	2	87
Benton	3			1			4
Boone	19			5	1	1	26
Carroll	8	1		2			11
Cass	33			7	1	1	42
Clark	86			3	2		91
Clay	11			1		1	13
Clinton	12			4			16
Daviess-Martin	13			5	2		20
Dearborn-Ohio	23	2		2			27
Decatur	8			3			11
DeKalb	15			4	1	1	21
Delaware-Blackford	132	8	2	18	4		164
Dubois	34	3		4		1	42
Elkhart	109	10	2	18	7	1	147
Fayette-Franklin	21			3	1	1	26
Floyd	64	2		4	2	1	73
Ft. Wayne-Allen	364	10	28	53	15	6	476
Fountain-Warren	8			3			11
Fulton	8			1			9
Gibson	8	1		3	1	1	14
Grant	72	1		19	2	1	95
Greene	11			6			17
Hamilton	30	1		1			32
Hancock	25	1		1	1	1	29
Harrison-Crawford	10	1				1	12
Hendricks	35			2			37
Henry	33			6		1	40
Howard	82	2		8	7	1	100
Huntington	17	2		4			23
Indianapolis-Marion	1318	41	39	184	51	21	1654
Jackson	19			5			24
Jennings	3			1			4
Jasper	9			1	1		11
Jay	18			2			20
Jefferson-Switzerland	30			5	2		37
Johnson	36	2		3	1		42
Knox	50	2		8	1	1	62
Kosciusko	25				1		26
LaGrange	9			1	1		11
Lake	563	5	1	66	18	2	655
LaPorte	97	5		10	2		114
Lawrence	40	5		1		1	47
Madison	114	3		17	5	4	143
Marshall	18	4	1	1			24
Miami	17			3			20
Montgomery	21	3		2	1		27
Morgan	13			4	2		19
Newton	4			2			6
Noble	14				1		15
Orange	4			2			6
Owen-Monroe	128	2	1	5	4	1	151
Parke-Vermillion	8			3	2		13
Perry	5			1			6
Pike	1						1
Porter	102	3		5	2		112
Posey	2	1		3			6
Pulaski	5			2			7
Putnam	12			2	1		15
Randolph	11			4		2	17
Ripley	8			1			9
Rush	9			5			14
St. Joseph	240	11		51	11	5	318
Scott	5	1		2			8
Shelby	18			3			21
Spencer	2			1			3
Starke	7			2			9
Steuben	11	1		3	2	1	18
Sullivan	7			5	1		13
Tippecanoe	172	5		27	3		207
Tipton	8	1		4			13
Vanderburgh	324	9	4	48	7	4	396
Vigo	129	2		19	7	2	159
Wabash	24	2		2			28
Warrick	12			1			13
Washington	6			1			7
Wayne-Union	74	5	1	12	4		96
Wells	41	3		9	2	2	57
White	6			4			10
Whitley	8			2	2	1	13
RMS			246				246
Totals	5183	162	326	757	187	69	6684

Giant Cell Arteritis of the Coronary Arteries

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SAEED T. VAKILI, M.D.[3]

Abstract

Atherosclerotic coronary artery disease is the major cause of coronary disease throughout the industrialized world. However, other acquired disease states may affect this important arterial system, including vasculitis. A case of giant cell arteritis involving the coronary arteries associated with sudden death is described. The clinical presentation, pathologic findings and treatment protocols are discussed.

GIANT CELL ARTERITIS is a well recognized, generalized vascular disease.[1] Major involvement of the arota and its branches have been reported; however, arteritic involvement of the coronary arteries is a rare occurrence.[1-15] The report that follows describes a case of giant cell arteritis involving exclusively the coronary arteries and aorta associated with sudden death.

Patient Description

A diabetic, hypertensive, demented 80-year-old man presented for evaluation of worsening mental status. Past medical history was significant for four cerebral vascular accidents. Physical examination revealed a dehydrated cachectic male with right hemiparesis and lower extremity edema. The temporal arteries were not palpable. A III/VI precordial systolic ejection murmur with S_4 gallop was appreciated on auscultation. Admitting abnormal laboratory studies included a glucose of 242 mg/dl and a platelet count of 606 x 10^9/L. A sedimentation rate was not obtained. Approximately 12 hours after admission, the patient was found without pulse or respiration. Despite resuscitative measures, he died.

At autopsy, the heart weighed 370 grams with a normal coronary artery distribution. Multiple sections of the left ventricle revealed numerous small muscle penetrating intramural coronary arteries involved by a granulomatous inflammatory process. The vessels contained numerous Langerhan's type giant cells within the media (*Fig. 1 & 2*). Elastic stains showed disruption of the internal elastic lamina by the giant cells. Acid-fast and fungal stains were negative for organisms. The intervening myocardium revealed focal cardiac fiber hypertrophy with perivascular fibrosis. The interstition was free of inflammation. Focal areas of the media of the major epicardial (extramural) coronary arteries contained patchy lymphocytic infiltrates with scattered giant cells. The circumflex artery showed total occlusion by atherosclerotic plaque and the remaining coronary vessels had luminal narrowing occlusion up to 75% in cross-sectional area by atherosclerotic plaque. The aortic arch contained patchy lymphocytic infiltrates without giant cells. The cerebral vessels and internal carotid arteries were normal. Tissue from temporal arteries was not available for histologic examination.

Other findings included severe atherosclerotic cerebrovascular disease with massive remote infarcts of the left inferior frontal gyrus, left parietal operculum, left deep white matter, left globus pallidus, left putamen and a portion of left internal capsule.

Incidental findings included slight emphysema, multiple granulomas of the liver, cholelithiasis, slight arteriolonephrosclerosis and nodular hyperplasia of the prostate.

Discussion

Giant cell arteritis (GCA) is a systemic disease that affects more than one percent of the elderly population.[13] It can be classified as classic or masked varieties.[16] The classic presentation represents the well recognized patterns of cranial arteritis and polymyalgia rheumatica with head pain, temporal tenderness, elevated sedimentation rates (ESR) and potential for acute blindness without treatment. Masked varieties of GCA include any atypical presentation including any of the above with focal neuralgia, polymyalgia or a pathologic mourning reaction.[17] Cardiac symptomatology within the group in-

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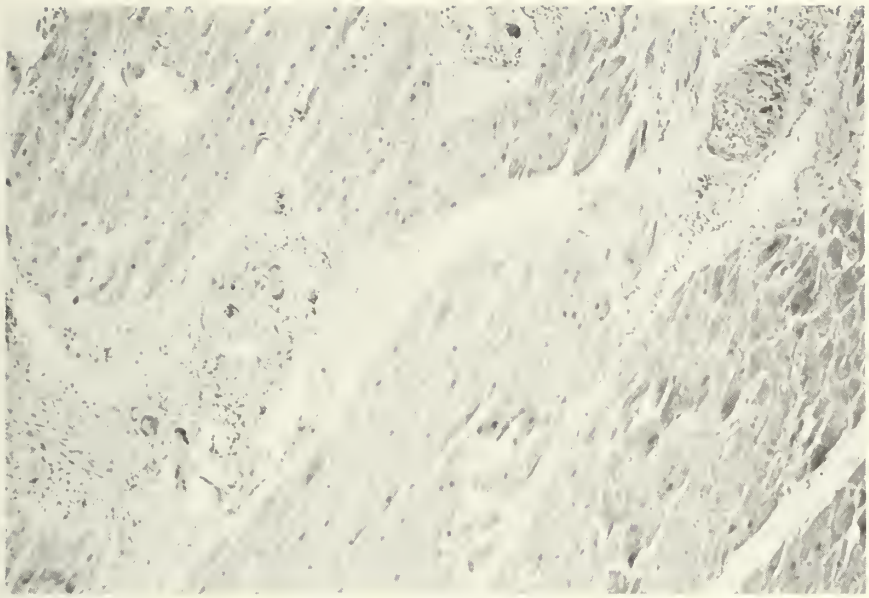


FIGURE 1: Multiple penetrating vessels with numerous giant cells in the media are shown. The surrounding myocardium is free of inflammation. (hematoxylin-eosin X40).

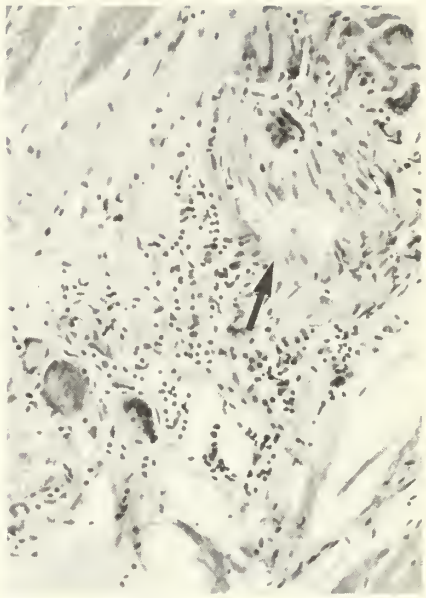


FIGURE 2: Multiple giant cells are shown within the media of two vessels. The larger vessel (arrow) shows luminal narrowing secondary to the granulomatous process. (hematoxylin-eosin X100).

cludes angina pectoris[18] with or without myocardial infarction,[3,6,7,8,10,15] aortic regurgitation,[19] and pericarditis.[20]

Sixteen previous cases of coronary artery involvement by GCA have been reported.[1-15] Widespread involvement of other arteries including the aorta,[3,4,5,7,8,11,14] temporal,[4,5,6,7,8,13,15] carotid,[1,4,5,7,8,10,11,12] renal,[2] subclavian,[3,12] bronchial,[4] ophthalmic,[6,7,8,10] superior mesentric,[2,12] iliac,[3,8] ovarian,[4] cerebral,[6,15] lingual,[7,22] and ciliary[8] is usually seen. Grossly, the arteries may appear normal or pearly white; flat intimal plaques may be apparent. Histologic studies reveal fibrosis of the intima with focal necrosis and a patchy chronic inflammatory infiltrate composed of small lymphocytes and plasma cells within the media. Giant cells are not necessary for the diagnosis of GCA. Their presence indicates active destruction of the internal elastic lamina, which is best seen with elastic stains. Immunoperoxidase staining for immunoglobulin reveals IgM deposits near the elastic lamina and within plasma cells.[15]

The majority of patients with GCA will have an elevated ESR at some time during the course of their disease; however, a normal ESR does not exclude GCA. A series of ESR may be necessary to establish this chronic inflammatory process.

A need for a more sensitive and specific test for GCA other than ESR and arterial biopsy exists, but present research into this area has not been fruitful. Angiographic studies may delineate features suggestive of arteritis, such as long smooth arterial stenosis with absence of irregular plaques and ulceration.[14]

Recognition that arteritis is the cause of cardiac symptoms is not easy and requires a high index of suspicion for appropriate therapy. Prednisone in high doses is the main treatment as outlined for polymyalgia rheumatica. Clinical suspicions may require temporal artery biopsy and coronary angiography for diagnosis and treatment of this insidious disease.

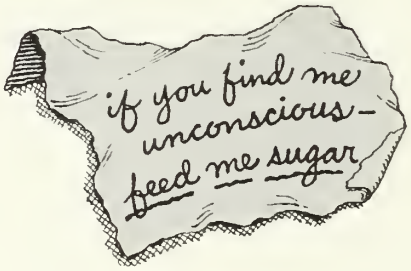
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Medicine's Lighter Moments

TED L. GRISELL, M.D.
Indianapolis



THE 'STREET BUM'

DURING A RAINY NIGHT in late September, a young man was brought in by ambulance to the emergency room of the old Indianapolis City Hospital. He had collapsed on a downtown street and wound up lying on a rain-clogged gutter.

Upon arrival, he was still unconscious and his clothing was wet and dirty. A casual examination of his clothing and contents revealed two or three pencilled notes on old brown wrapping paper that read, "If you find me unconscious, feed me sugar."

Because of these notes, the emergency room resident quickly ordered a blood sugar test; an IV of concentrated glucose was soon initiated.

The emergency room resident had once played for a professional football team, then located in Brooklyn, N.Y. He had all the characteristics of a football player—size, musculature, rough-and-ready demeanor, etc. As he pumped the sugar in, the patient began to respond and soon opened his eyes. He seemed to be aware of his surroundings.

As the doctor finished his work and withdrew the needle, he said to the patient, "What's the matter, Bud, your pancreas kicking up a fuss?"

Much to our surprise and delight, the young man replied, "No, Doctor. Due to the fact I have evidence of diabetes insipidus, they believe that my problem may be more of a pituitary dyscrasia."

Suffice it to say that we discovered the patient had been a medical student who had dropped out of medical school but who had obtained the degree of R.N. from a Philadelphia hospital.

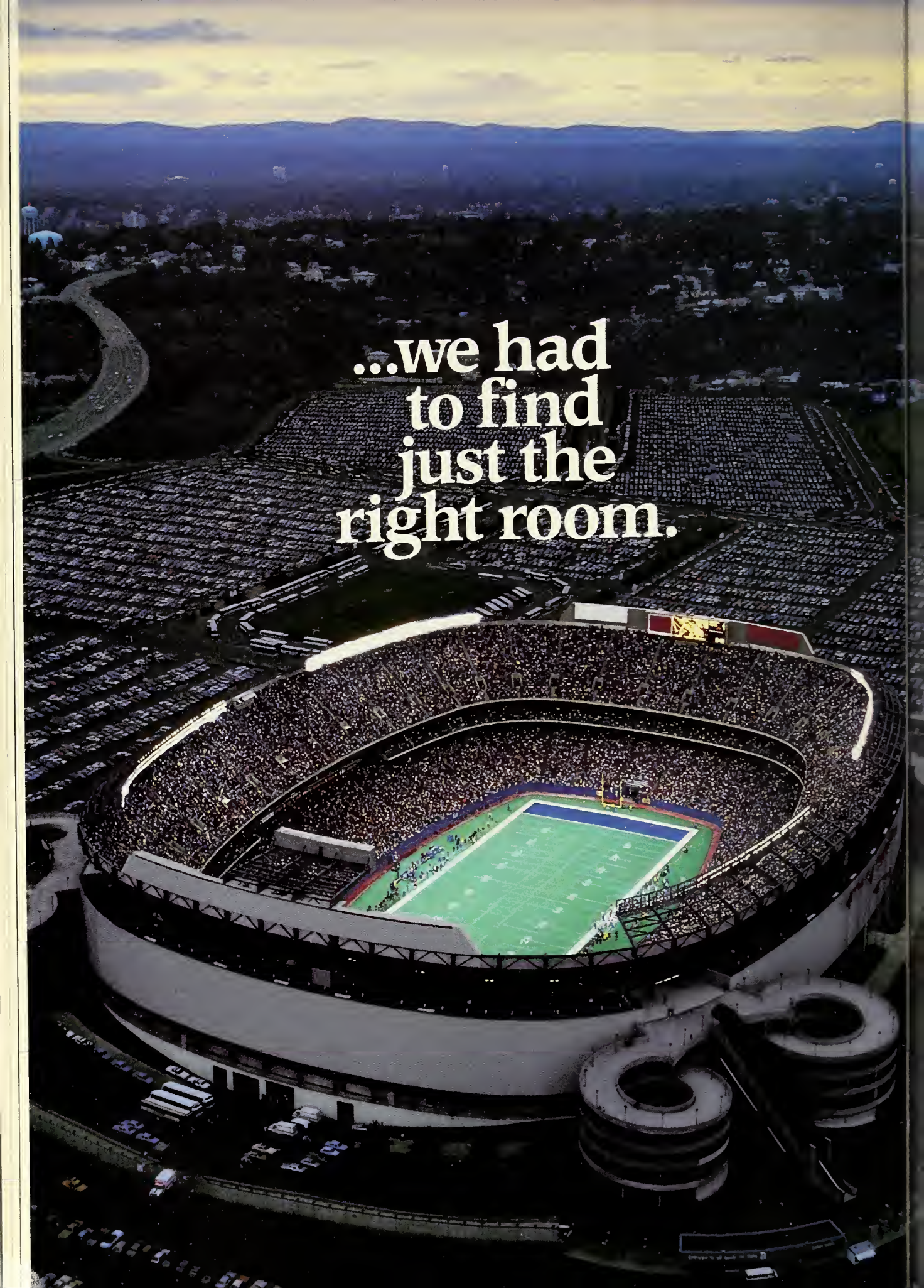
What had led to the young man's present situation was the fact that he had accepted a new position in a Kansas City, Mo. hospital and had elected to hitchhike there from Philadelphia. He had hitched a ride with a truck driver who was on a tight schedule. By the time he arrived in Indianapolis, he hadn't eaten adequately for about 24 hours. His blood sugar became so low as a result of his disorder that he became unconscious with a hypoglycemic reaction.

And when he regained consciousness and offered a startling professional explanation of his problem, he created an emergency room episode that has not been forgotten.

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...we had
to find
just the
right room.

60,073 patients (90%) who started on INDERAL® LA stayed on INDERAL LA.[1*]

Surprising? Not really.

Because most patients on INDERAL LA (propranolol HCl) don't even know it's working.
A recent double-blind, placebo-controlled, crossover study in 138 hypertensive patients[2] revealed that INDERAL LA has a side effects profile unsurpassed by atenolol or metoprolol—which shows how well-tolerated once-daily INDERAL LA can be.

Sole therapy or concomitant therapy? Fifty-nine percent of the time, INDERAL LA stood on its own.

The patients in the nationwide compliance trial were no different from yours. Generally when the antihypertensive regimen is complicated, compliance may become a problem. So, the effectiveness of INDERAL LA as once-daily monotherapy is a big plus. Of the remaining hypertensives in the program, 36% were controlled merely with the addition of a diuretic to INDERAL LA.

For the noncompliant patients in your practice, INDERAL LA may well be the answer.

Almost 20,000 of the patients in the nationwide compliance trial were identified as having been noncompliant with their previous antihypertensive therapy. Their physicians reported that 88% showed improved compliance when placed on once-daily INDERAL LA.

Control, comfort, and compliance

ONCE-DAILY
INDERAL® LA
(PROPRANOLOL HCl)
LONG ACTING CAPSULES

Like conventional INDERAL Tablets, INDERAL LA should not be used in the presence of congestive heart failure, sinus bradycardia, cardiogenic shock, heart block greater than first degree, and bronchial asthma.

*After a 30-day trial with INDERAL LA, physicians reported that 90% of the patients would remain on INDERAL LA.

The one you know best keeps looking better

Please see next page for brief summary of prescribing information

The one you know best keeps looking better

BRIEF SUMMARY *(FOR FULL PRESCRIBING INFORMATION, SEE PACKAGE CIRCULAR.)*

INDERAL® LA brand of propranolol hydrochloride **(Long Acting Capsules)**

DESCRIPTION. Inderal LA is formulated to provide a sustained release of propranolol hydrochloride. Inderal LA is available as 80 mg, 120 mg, and 160 mg capsules.

CLINICAL PHARMACOLOGY. INDERAL is a nonselective beta-adrenergic receptor blocking agent possessing no other autonomic nervous system activity. It specifically competes with beta-adrenergic receptor stimulating agents for available receptor sites. When access to beta-receptor sites is blocked by INDERAL, the chronotropic, inotropic, and vasodilator responses to beta-adrenergic stimulation are decreased proportionately.

INDERAL LA Capsules (80, 120, and 160 mg) release propranolol HCl at a controlled and predictable rate. Peak blood levels following dosing with INDERAL LA occur at about 6 hours and the apparent plasma half-life is about 10 hours. When measured at steady state over a 24-hour period the areas under the propranolol plasma concentration-time curve (AUCs) for the capsules are approximately 60% to 65% of the AUCs for a comparable divided daily dose of INDERAL tablets. The lower AUCs for the capsules are due to greater hepatic metabolism of propranolol, resulting from the slower rate of absorption of propranolol. Over a twenty-four (24) hour period, blood levels are fairly constant for about twelve (12) hours then decline exponentially.

INDERAL LA should not be considered a simple mg for mg substitute for conventional propranolol and the blood levels achieved do not match (are lower than) those of two to four times daily dosing with the same dose. When changing to INDERAL LA from conventional propranolol, a possible need for retitration upwards should be considered especially to maintain effectiveness at the end of the dosing interval. In most clinical settings, however, such as hypertension or angina where there is little correlation between plasma levels and clinical effect, INDERAL LA has been therapeutically equivalent to the same mg dose of conventional INDERAL as assessed by 24-hour effects on blood pressure and on 24-hour exercise responses of heart rate, systolic pressure and rate pressure product. INDERAL LA can provide effective beta blockade for a 24-hour period.

The mechanism of the antihypertensive effect of INDERAL has not been established. Among the factors that may be involved in contributing to the antihypertensive action are (1) decreased cardiac output, (2) inhibition of renin release by the kidneys, and (3) diminution of tonic sympathetic nerve outflow from vasomotor centers in the brain. Although total peripheral resistance may increase initially, it readjusts to or below the pretreatment level with chronic use. Effects on plasma volume appear to be minor and somewhat variable. INDERAL has been shown to cause a small increase in serum potassium concentration when used in the treatment of hypertensive patients.

In angina pectoris, propranolol generally reduces the oxygen requirement of the heart at any given level of effort by blocking the catecholamine-induced increases in the heart rate, systolic blood pressure, and the velocity and extent of myocardial contraction. Propranolol may increase oxygen requirements by increasing left ventricular fiber length, end diastolic pressure and systolic ejection period. The net physiologic effect of beta-adrenergic blockade is usually advantageous and is manifested during exercise by delayed onset of pain and increased work capacity.

In dosages greater than required for beta blockade, INDERAL also exerts a quinidine-like or anesthetic-like membrane action which affects the cardiac action potential. The significance of the membrane action in the treatment of arrhythmias is uncertain.

The mechanism of the antimigraine effect of propranolol has not been established. Beta-adrenergic receptors have been demonstrated in the pial vessels of the brain.

Beta receptor blockade can be useful in conditions in which, because of pathologic or functional changes, sympathetic activity is detrimental to the patient. But there are also situations in which sympathetic stimulation is vital. For example, in patients with severely damaged hearts, adequate ventricular function is maintained by virtue of sympathetic drive which should be preserved. In the presence of AV block, greater than first degree, beta blockade may prevent the necessary facilitating effect of sympathetic activity on conduction. Beta blockade results in bronchial constriction by interfering with adrenergic bronchodilator activity which should be preserved in patients subject to bronchospasm.

Propranolol is not significantly dialyzable.



INDICATIONS AND USAGE. Hypertension: INDERAL LA is indicated in the management of hypertension; it may be used alone or used in combination with other antihypertensive agents, particularly a thiazide diuretic. INDERAL LA is not indicated in the management of hypertensive emergencies.

Angina Pectoris Due to Coronary Atherosclerosis: INDERAL LA is indicated for the long-term management of patients with angina pectoris.

Migraine: INDERAL LA is indicated for the prophylaxis of common migraine headache. The efficacy of propranolol in the treatment of a migraine attack that has started has not been established and propranolol is not indicated for such use.

Hypertrophic Subaortic Stenosis: INDERAL LA is useful in the management of hypertrophic subaortic stenosis, especially for treatment of exertional or other stress-induced angina, palpitations, and syncope. INDERAL LA also improves exercise performance. The effectiveness of propranolol hydrochloride in this disease appears to be due to a reduction of the elevated outflow pressure gradient which is exacerbated by beta-receptor stimulation. Clinical improvement may be temporary.

CONTRAINDICATIONS. INDERAL is contraindicated in 1) cardiogenic shock, 2) sinus bradycardia and greater than first degree block, 3) bronchial asthma, 4) congestive heart failure (see WARNINGS) unless the failure is secondary to a tachyarrhythmia treatable with INDERAL.

WARNINGS. CARDIAC FAILURE. Sympathetic stimulation may be a vital component supporting circulatory function in patients with congestive heart failure, and its inhibition by beta blockade may precipitate more severe failure. Although beta blockers should be avoided in overt congestive heart failure, if necessary, they can be used with close follow-up in patients with a history of failure who are well compensated and are receiving digitalis and diuretics. Beta-adrenergic blocking agents do not abolish the inotropic action of digitalis on heart muscle.

IN PATIENTS WITHOUT A HISTORY OF HEART FAILURE, continued use of beta blockers can, in some cases, lead to cardiac failure. Therefore, at the first sign or symptom of heart failure, the patient should be digitalized and/or treated with diuretics, and the response observed closely or INDERAL should be discontinued (gradually, if possible).

IN PATIENTS WITH ANGINA PECTORIS, there have been reports of exacerbation of angina and, in some cases, myocardial infarction, following abrupt discontinuance of INDERAL therapy. Therefore, when discontinuance of INDERAL is planned the dosage should be gradually reduced over at least a few weeks, and the patient should be cautioned against interruption or cessation of therapy without the physician's advice. If INDERAL therapy is interrupted and exacerbation of angina occurs, it usually is advisable to reinstitute INDERAL therapy and take other measures appropriate for the management of unstable angina pectoris. Since coronary artery disease may be unrecognized, it may be prudent to follow the above advice in patients considered at risk of having occult atherosclerotic heart disease who are given propranolol for other indications.

Nonallergic Bronchospasm (e.g., chronic bronchitis, emphysema) — PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD IN GENERAL NOT RECEIVE BETA BLOCKERS. INDERAL should be administered with caution since it may block bronchodilation produced by endogenous and exogenous catecholamine stimulation of beta receptors.

MAJOR SURGERY. The necessity or desirability of withdrawal of beta-blocking therapy prior to major surgery is controversial. It should be noted, however, that the impaired ability of the heart to respond to reflex adrenergic stimuli may augment the risks of general anesthesia and surgical procedures.

INDERAL (propranolol HCl), like other beta blockers, is a competitive inhibitor of beta-receptor agonists and its effects can be reversed by administration of such agents, e.g., dobutamine or isoproterenol. However, such patients may be subject to protracted severe hypotension. Difficulty in starting and maintaining the heartbeat has also been reported with beta blockers.

DIABETES AND HYPOGLYCEMIA. Beta-adrenergic blockade may prevent the appearance of certain premonitory signs and symptoms (pulse rate and pressure changes) of acute hypoglycemia in labile insulin-dependent diabetes. In these patients, it may be more difficult to adjust the dosage of insulin.

THYROTOXICOSIS. Beta blockade may mask certain clinical signs of hyperthyroidism. Therefore, abrupt withdrawal of propranolol may be followed by an exacerbation of symptoms of hyperthyroidism, including thyroid storm. Propranolol does not distort thyroid function tests.

IN PATIENTS WITH WOLFF-PARKINSON-WHITE SYNDROME, several cases have been reported in which, after propranolol, the tachycardia was replaced by a severe bradycardia requiring a demand pacemaker. In one case, this resulted after an initial dose of 5 mg propranolol.

PRECAUTIONS. *General.* Propranolol should be used with caution in patients with impaired hepatic or renal function. INDERAL (propranolol HCl) is not indicated for the treatment of hypertensive emergencies.

Beta-adrenoreceptor blockade can cause reduction of intraocular pressure. Patients should be told that INDERAL may interfere with the glaucoma screening test. Withdrawal may lead to return of increased intraocular pressure.

Clinical Laboratory Tests. Elevated blood urea levels in patients with severe heart disease, elevated serum transaminase, alkaline phosphatase, lactate dehydrogenase.

DRUG INTERACTIONS. Patients receiving catecholamine-depleting drugs such as reserpine should be closely observed if INDERAL is administered. The added catecholamine-blocking action may produce an excessive reduction of resting sympathetic nervous activity which may result in hypotension, marked bradycardia, vertigo, syncopal attacks, or orthostatic hypotension.

Carcinogenesis, Mutagenesis, Impairment of Fertility. Long-term studies in animals have been conducted to evaluate toxic effects and carcinogenic potential. In 18-month studies in both rats and mice, employing doses up to 150 mg/kg/day, there was no evidence of significant drug-induced toxicity. There were no drug-related tumorigenic effects at any of the dosage levels. Reproductive studies in animals did not show any impairment of fertility that was attributable to the drug.

Pregnancy. Pregnancy Category C. INDERAL has been shown to be embryotoxic in animal studies at doses about 10 times greater than the maximum recommended human dose.

There are no adequate and well-controlled studies in pregnant women. INDERAL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. INDERAL is excreted in human milk. Caution should be exercised when INDERAL is administered to a nursing woman.

Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS. Most adverse effects have been mild and transient and have rarely required the withdrawal of therapy.

Cardiovascular. bradycardia, congestive heart failure, intensification of AV block, hypotension, paresthesia of hands, thrombocytopenic purpura, arterial insufficiency usually of the Raynaud type.

Central Nervous System. lightheadedness, mental depression manifested by insomnia, lassitude, weakness, fatigue, reversible mental depression progressing to catatonia, visual disturbances, hallucinations, an acute reversible syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability, slightly clouded sensorium, and decreased performance on neuropsychometrics.

Gastrointestinal. nausea, vomiting, epigastric distress, abdominal cramping, diarrhea, constipation, mesenteric arterial thrombosis, ischemic colitis.

Allergic. pharyngitis and agranulocytosis, erythematous rash, fever combined with aching and sore throat, laryngospasm and respiratory distress.

Respiratory. bronchospasm.

Hematologic. agranulocytosis, nonthrombocytopenic purpura, thrombocytopenic purpura.

Auto-Immune. In extremely rare instances, systemic lupus erythematosus has been reported.

Miscellaneous. alopecia. LE-like reactions, psoriasiform rashes, dry eyes, male impotence, and Peyronie's disease have been reported rarely. Oculomucocutaneous reactions involving the skin, serous membranes and conjunctivae reported for a beta blocker (practolol) have not been associated with propranolol.

DOSAGE AND ADMINISTRATION. INDERAL LA provides propranolol hydrochloride in a sustained-release capsule for administration once daily. If patients are switched from INDERAL tablets to INDERAL LA capsules, care should be taken to assure that the desired therapeutic effect is maintained. INDERAL LA should not be considered a simple mg for mg substitute for INDERAL. INDERAL LA has different kinetics and produces lower blood levels. Retitration may be necessary especially to maintain effectiveness at the end of the 24-hour dosing interval.

HYPERTENSION — *Dosage must be individualized.* The usual initial dosage is 80 mg INDERAL LA once daily, whether used alone or added to a diuretic. The dosage may be increased to 120 mg once daily or higher until adequate blood-pressure control is achieved. The usual maintenance dosage is 120 to 160 mg once daily. In some instances a dosage of 640 mg may be required. The time needed for full hypertensive response to a given dosage is variable and may range from a few days to several weeks.

ANGINA PECTORIS — *Dosage must be individualized.* Starting with 80 mg INDERAL LA once daily, dosage should be gradually increased at three to seven day intervals until optimum response is obtained. Although individual patients may respond at any dosage level, the average optimum dosage appears to be 160 mg once daily. In angina pectoris, the value and safety of dosage exceeding 320 mg per day have not been established.

If treatment is to be discontinued, reduce dosage gradually over a period of a few weeks (see WARNINGS).

MIGRAINE — *Dosage must be individualized.* The initial oral dose is 80 mg INDERAL LA once daily. The usual effective dose range is 160-240 mg once daily. The dosage may be increased gradually to achieve optimum migraine prophylaxis. If a satisfactory response is not obtained within four to six weeks after reaching the maximum dose, INDERAL LA therapy should be discontinued. It may be advisable to withdraw the drug gradually over a period of several weeks.

HYPERTROPHIC SUBAORTIC STENOSIS — 80-160 mg INDERAL LA once daily.

PEDIATRIC DOSAGE — At this time the data on the use of the drug in this age group are too limited to permit adequate directions for use.

*The appearance of these capsules is a registered trademark of Ayerst Laboratories.

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THE FINNERAN PROFESSORSHIP

St. Vincent Hospital Names Polish Surgeon as 1987 Visiting Professor

AUSTIN L. GARDNER, M.D.
Indianapolis

THE JOSEPH C. FINNERAN Professorship Committee has announced that Professor Witold J. Rudowski, M.D., of Warsaw, Poland will be the 1987 Visiting Professor. Professor Rudowski, renowned for his work in the surgical care of hemophiliac patients and problems of hemostasis and coagulation in surgery, will be the seventh in the line of distinguished international surgeons brought to Indianapolis by the Finneran Professorship.

The Joseph C. Finneran Surgical Educational Endowment Fund was established in April 1980 by Sister Theresa Peck and Doctors Harris B Shumacker and Robert F. Nagan of St. Vincent Hospital shortly before the death of Doctor Finneran.



Doctor Finneran

Doctor Finneran had come to Indianapolis from Johns Hopkins Hospital at the request of Doctor Shumacker when he assumed the Professorship of Surgery at Indiana University School of Medicine. On completion of his residency training and after service with the Armed Forces in Europe, Doctor Finneran became chairman of the Surgical Service at St. Vincent Hospital. In this role, he succeeded Doctor Willis O. Gatch, who himself had come to Indiana after residency training at Johns Hopkins under the famous Doctor William Halstead.

The roster of internationally renowned surgeons for the professorship speaks for the global contacts of Doctor Shumacker, Emeritus Distinguished Professor of Surgery at Indiana University School of Medicine, and currently Professor and Senior Advisor of the Uniformed Services University in Bethesda.

The first visiting lecturer was Professor Maurice Mercadier, an eminent French surgeon and chief of the American Hospital in Paris and l'Hôpital de la Pieté in Paris, who is especially noted for his reputation in surgical problems of the pancreas, liver and biliary system. The late Professor John E. Jesseph presided over these presentations and discussion of sphincteroplasty conducted at the Indiana University School of Medicine. Subsequently, Professor A.P.M. Forrest, the Regius Professor of Clinical Surgery at the University of Edinburgh, discussed "Hormones and Their Implication in the Managment of Breast Cancer." At the evening banquet, a delightful note was struck when he entertained the audience with a review of the history of the body snatchers of Edinburgh, noting that the famous Mr. Burke made the mistake of "doing in" a well known prostitute.

In 1983, Professor Sven-Eric Bergentz, Chairman of Surgery at the University of Lund and Chief of Surgery at Malmö General Hospital in Sweden, reviewed the "Surgery of Renal Arteries," "Surgery of Patients With Bleeding Disorders" and finally, "Post-Operative Thromboembolism." The program also included Doctor Nils Bang's discussion of "Thrombolysis." Doctor Maurice Arregui's presentation, "Arguments for Splenic Preservation," and Doctor William Wahle's

When and Where

The program for this year's Finneran lecture—the theme is "Surgical Hemostasis and Transfusion"—will begin at 9 a.m., Friday, May 1, at St. Vincent Hospital and conclude at 10:30 a.m., Saturday, May 2 at Wishard Memorial Hospital.

The program is designed to be of particular usefulness to those engaged in family practice, internal medicine, obstetrics and gynecology, blood banks, and the surgical specialists.

For additional information about the program, contact Marilyn Soltermann, CME coordinator at St. Vincent Hospital—(317) 871-3460.

"Newer Concepts of the Progression of Carotid Stenosis" were also given.

In 1984 Professor Richard B. Welbourn of the Royal Postgraduate Medical School at Hammersmith Hospital in London was the fourth visiting professor. Professor Welbourn, a Hunterian Professor, a former Fulbright Scholar, and a founding member of the International Association of Endocrine Surgeons, discussed "Neuroendocrine Tumors of the Gut" and "Adrenal Tumors."

The fifth visiting lecturer was Doctor Gunnar Nylander, who in 1985 reviewed "Progress in Colorectal Cancer Over a Thirty-Year Period." In the program, chaired by Doctors Robert F. Nagan and Jay Grosfeld, Chief of Surgery, Indiana University School of Medicine, topics included "Fluid Shifts in Early Hemorrhage" and "Colon Surgery in Infancy and Childhood." In his review, Doctor Grosfeld paid tribute to the Scandinavian surgeons for their outstanding contribution to the development of colon surgery on infants and children. The program included a workshop on "Lasers in General Surgery."

In May 1986 Professor Hans G. Borst of Hannover, Germany, who received his medical degree from Harvard Medical School, discussed "Surgery for Aneurysms and Dissection of the Ascending Aorta." Doctor Shumacker then reviewed "The History of Cardiac Surgery" and in an evening session at the Children's Museum, Doctor Borst discussed "Heart Transplantation in Europe." During the Saturday morning session at Indiana University Medical Center, Doctor Yousuf Mahomed reviewed problems of "Cardiac Mapping," Doctor John Brown discussed "Apical Aortic Conduit," and Doctor Kathleen Reilly presented a paper on "Spinal Cord Ischemia." Doctor Malcolm Herring reviewed his work in "Endothelial Seeding."

About the Professor



Witold J. Rudowski, M.D.

The 1987 Finneran Professor, Witold J. Rudowski, M.D., is Director and Head of the Department of Surgery, Research Institute of Hematology and Blood Transfusion, Warsaw, Poland. He is also Professor of Surgery at the University of Warsaw.

Dr. Rudowski, who was born in Piotrkow, Poland, was educated at Mickiewicz College in Warsaw. He attended the University of Warsaw and the Clandestine Warsaw University Medical School. He subsequently attended the Postgraduate Medical School at the University of London and received an American Cancer Society fellowship in 1963. In the past he has been a visiting scientist at the National Institutes of Health.

In addition to his surgical and teaching duties, Dr. Rudowski serves as Deputy Secretary of the Section of the Medical Sciences at the Polish Academy of Sciences in Warsaw, and he is a member of the Scientific Council to the Minister of Health and Social Welfare. He is the national and head delegate of Poland to the World Health Assemblies and is a member of the Executive Board of the World Health Organization.

Dr. Rudowski's professional affiliations include the International Surgical Society, International Society of Hematology and Blood Transfusion, and the International Society for Burn Injury. He is an honorary member of the Hungarian Society of Hematology and Blood Transfusion, and is an honorary fellow of both the American College of Surgeons and the Royal College of Surgeons of England. He is a national delegate and past president of the International Federation of Surgical Colleges.

Dr. Rudowski's areas of research and clinical practice have concentrated on blood transfusion services and blood products—with particular reference to the transmission of AIDS—and surgical and rehabilitative technology. He is the author of several books and has published more than 400 scientific articles, in various languages. He is a member of the editorial boards of the *World Journal of Surgery*, the *American Journal of Surgery*, and the *International Journal of Medical Research*.

Schedule of Events

Friday, May 1
Moderator, Morning Session: Austin L. Gardner, M.D.

9:00 ..... Registration and Coffee
9:25 ..... Welcome—Bain J. Farris, President
9:30 ..... Introduction of Professor Rudowski by Harris B Shumacker Jr., M.D.
9:35 ..... Seventh Annual Joseph C. Finneran Lecture "Surgery in Patients with Congenital Coagulopathies," Witold J. Rudowski, M.D.
10:30 ..... Case Presentation: Disseminated Intravascular Coagulation Secondary to Sepsis: Mary C. McCarthy, M.D.
11:00 ..... Case Presentation: New Guidelines for Use of Conventional Anticoagulants: Nils U. Bang, M.D., Ph.D.
11:30 ..... Case Presentation: Emergency Surgery in the Presence of Anti-platelet Drugs: Malcolm B. Herring, M.D.
Noon ..... Panel: Drs. Rudowski, McCarthy, Bang, Herring
12:30 ..... Lunch (Brief history of the Clandestine Warsaw University—Dr. Rudowski)

Friday, May 1
Moderator, Afternoon Session: Maurice E. Arregui, M.D.

1:30 ..... Accessory Spleens: Clinical Significance with Particular Reference to the Recurrence of Idiopathic Thrombocytopenic Purpura: Professor Rudowski
2:15 ..... Case Presentation: New Approach in Antithrombotic Therapy Using Recombinant D.N.A. Technology: Nils U. Bang, M.D., Ph.D.
3:00 ..... Case Presentation: Significant Complications of Blood Transfusion and Alternatives to Traditional Forms of Hemotherapy: Victor H. Muller, M.D.
3:45 ..... Case Presentation: Work-up and Treatment of Coagulopathy Associated with Massive Transfusion: George Rodman, M.D.
4:15 ..... Panel: Drs. Rudowski, Bang, Muller, Rodman
4:30 ..... Adjourn
6:30 ..... Cocktails, Woodstock Country Club
7:30 ..... Dinner (Speaker: Professor Rudowski on "Nicolaus Copernicus as Physician")

Saturday, May 2
Moderator: Mary C. McCarthy, M.D.

8:00 ..... Autotransfusion in Trauma
Thomas A. Broadie, M.D.
8:30 ..... Component Therapy in Massive Blood Loss
Leo J. McCarthy, M.D.
9:00 ..... Blood Transfusion: Yesterday, Today and Tomorrow
Professor Rudowski
10:30 ..... Adjourn

What Happens to the Finneran Professors?

HARRIS B SHUMACKER, M.D.
Bethesda, Md.

The world renowned surgeons who have visited Indianapolis in order to honor the name of Joseph C. Finneran have contributed immensely to the annual events sponsored by the Joseph C. Finneran Surgical Educational Fund. They have brought with them lifetimes of experience in teaching, clinical surgical care, and investigative work. They and their wives have afforded us great pleasure and have become warm friends of many who had the opportunity of being with them. How have they fared since their departure?

Professor Maurice Mercadier has retired from his dual role as chief of service at La Pieté and the American Hospital but continues to be very active, writing a book, attending to his obligations to such organizations as the Societé Internationale de Chirurgie, and to other professional matters. He still lives in Paris and has time on occasions to be with his friend Charles Dubost on his farm in the south of France.

Professor Sir Patrick Forrest will soon retire from his post in Edinburgh. Rumor has it that he will then move to a warmer place. His *Principles and Practice of Surgery*, published in 1985, enjoyed such success it had to be reprinted the same year. He weathered a myocardial infarction so well he appears fit to dance to Scottish bagpipes in kilts on a winter day. Everyone is overjoyed by his elevation to Knighthood.

From the Edward Hebert School of Medicine, the Uniformed Services University of the Health Sciences, Bethesda, Md.

Professor Sven-Eric Bergentz pursues his extraordinarily busy and productive life in Malmö, writes extensively about his important research projects, serves actively in numerous professional organizations, and upon various national committees. His worldwide travels often bring him to the States.

Professor Richard Welbourn has also retired from his position at the Royal Postgraduate Medical School, but can be found there almost daily busily engaged in writing what is surely destined to be for all times the definitive history of endocrine surgery. His revised and enlarged *Dictionary of Medical Ethics* has been received enthusiastically. He lives in Surrey, not far from his old home in Kew Gardens.

Professor Gunnar Nylander is another recent retiree. He still has an office in the Karolinska where he is trying to catch up on the many things his previous activities made impossible. His replacement operations have abolished all his former physical handicaps. He enjoys his home in the country surrounded by members of his family who live on the property nearby.

Professor Hans Borst is as occupied as ever at Hannover, administering his very active department, attending to one of the world's largest cardiac surgical services, carrying out investigative work and reporting his observations, and fulfilling visiting professorships for which he is in constant demand.

A word about future Visiting Professors seems in order. Professor Witold Rudowski has recently returned to his duties in Warsaw after a busy and fruitful year as Visiting Scholar at the National Library of Medicine and as Visiting Professor at the Uniformed Services University of the Health Sciences. His far-reaching professional activities continue. He will make significant contributions to the next annual symposium.

Fortunately, it has been possible to arrange well ahead of time for the Finneran Visiting Professorship of 1988. A treat is in store for us as Sir Geoffrey Slaney of Birmingham will serve in this role. He has just finished his tenure in the highly honored and time-consuming position of president of the Royal College of Surgeons of England.

The wives cannot be forgotten! Lilliane Mercadier, Lady Margaret Forrest, Kerstin Bergentz, Rachel Welbourn, Karin Nylander, and Petra Borst are all well, busy, and happy. Irene Rudowski is not well enough to make the trip with her husband and will be missed. Lady Jo Slaney will be heartily welcomed next year.

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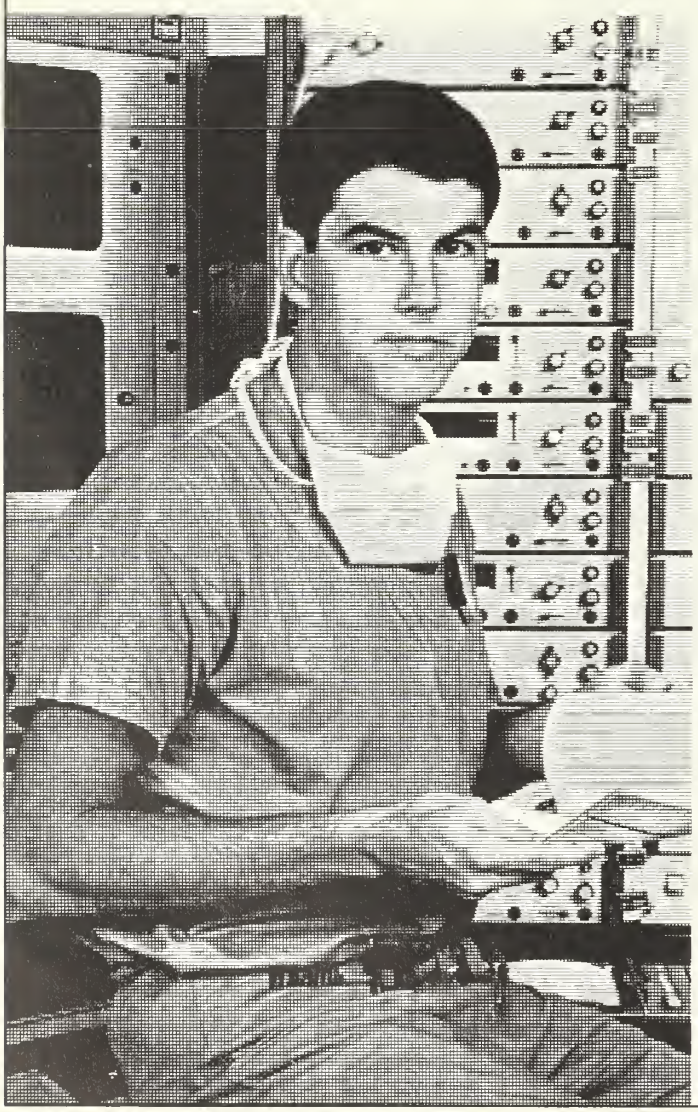
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Medical Malpractice Defense:
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MICROBIOLOGY The bactericidal activity of ceftriaxone results from inhibition of cell wall synthesis Ceftriaxone has a high degree of stability in the presence of beta lactamases, both penicillinases and cephalosporinases, of gram negative and gram positive bacteria Ceftriaxone is usually active against the following microorganisms *in vitro* and in clinical infections (see Indications and Usage)

GRAM NEGATIVE AEROBES: *Enterobacter aerogenes, Enterobacter cloacae, Escherichia coli, Haemophilus influenzae* (including ampicillin-resistant strains), *H parainfluenzae, Klebsiella* species (including *K pneumoniae*) *Neisseria gonorrhoeae* (including penicillinase and nonpenicillinase producing strains) *Neisseria meningitidis, Proteus mirabilis, Proteus vulgaris, Morganella morganii* and *Serratia marcescens*

Note: Many strains of the above organisms that are multiply resistant to other antibiotics, e.g., penicillins, cephalosporins and aminoglycosides, are susceptible to ceftriaxone sodium

Ceftriaxone is also active against many strains of *Pseudomonas aeruginosa*

GRAM POSITIVE AEROBES: *Staphylococcus aureus* (including penicillinase-producing strains) and *Staphylococcus epidermidis* (Note: methicillin resistant staphylococci are resistant to cephalosporins, including ceftriaxone), *Streptococcus pyogenes* (Group A beta-hemolytic streptococci), *Streptococcus agalactiae* (Group B streptococci) and *Streptococcus pneumoniae* (Note: Most strains of enterococci, *Streptococcus faecalis* and Group D streptococci are resistant.)

Ceftriaxone also demonstrates *in vitro* activity against the following microorganisms, although the clinical significance is unknown:

GRAM-NEGATIVE AEROBES: *Citrobacter freundii, Citrobacter diversus, Providencia* species (including *Providencia rettgeri*), *Salmonella* species (including *S typhi*), *Shigella* species and *Acinetobacter calcoaceticus*

ANAEROBES: *Bacteroides* species, *Clostridium* species (Note: most strains of *C difficile* are resistant)

SUSCEPTIBILITY TESTING: Standard susceptibility disk method: Quantitative methods that require measurement of zone diameters give the most precise estimate of antibiotic susceptibility. One such procedure (Bauer AW, Kirby WMM, Sherris JC, Turck M: Antibiotic Susceptibility Testing by a Standardized Single Disk Method, *Am J Clin Pathol* 45: 493-496, 1966; Standardized Disk Susceptibility Test *Federal Register* 39: 19182-19184, 1974, National Committee for Clinical Laboratory Standards, Approved Standard ASM 2, Performance Standards for Antimicrobial Disk Susceptibility Tests, July 1975) has been recommended for use with disks to test susceptibility to ceftriaxone.

Laboratory results of the standardized single disk susceptibility test using a 30-mcg ceftriaxone disk should be interpreted according to the following three criteria:

1. Susceptible organisms produce zones of 18 mm or greater, indicating that the tested organism is likely to respond to therapy.
2. Organisms that produce zones of 14 to 17 mm are expected to be susceptible if a high dosage (not to exceed 4 gm per day) is used or if the infection is confined to tissues and fluids (e.g., urine), in which high antibiotic levels are attained.
3. Resistant organisms produce zones of 13 mm or less, indicating that other therapy should be selected.

Organisms should be tested with the ceftriaxone disk since ceftriaxone has been shown by *in vitro* tests to be active against certain strains found resistant to cephalosporin class disks.

Organisms having zones of less than 18 mm around the cephalothin disk are not necessarily of intermediate susceptibility or resistant to ceftriaxone.

Standardized procedures require use of control organisms. The 30-mcg ceftriaxone disk should give zone diameters between 29 and 35 mm, 22 and 28 mm and 17 and 23 mm for the reference strains *E coli* ATCC 25922, *S aureus* ATCC 25923 and *P aeruginosa* ATCC 27853, respectively.

DILUTION TECHNIQUES: Based on the pharmacokinetic profile of ceftriaxone, a bacterial isolate may be considered susceptible if the MIC value for ceftriaxone is not more than 16 mcg/ml. Organisms are considered resistant to ceftriaxone if the MIC is equal to or greater than 64 mcg/ml. Organisms having an MIC value of less than 64 mcg/ml, but greater than 16 mcg/ml, are expected to be susceptible if a high dosage (not to exceed 4 gm per day) is used or if the infection is confined to tissues and fluids (e.g., urine) in which high antibiotic levels are attained.

E coli ATCC 25922, *S aureus* ATCC 25923 and *P aeruginosa* ATCC 27853 are also the recommended reference strains for controlling ceftriaxone dilution tests. Greater than 95% of MICs for the *E coli* strain should fall within the range of 0.016 to 0.5 mcg/ml. The range for the *S aureus* strain should be 1 to 2 mcg/ml, while for the *P aeruginosa* strain the range should be 8 to 64 mcg/ml.

INDICATIONS AND USAGE: Rocephin is indicated for the treatment of the following infections when caused by susceptible organisms:

LOWER RESPIRATORY TRACT INFECTIONS caused by *Strep pneumoniae, Streptococcus* species (excluding enterococci), *Staph aureus, H influenzae, H parainfluenzae, Klebsiella* species (including *K pneumoniae*), *E coli, E aerogenes, Proteus mirabilis* and *Serratia marcescens*

SKIN AND SKIN STRUCTURE INFECTIONS caused by *Staph aureus, Staph epidermidis, Streptococcus* species (excluding enterococci), *E cloacae, Klebsiella* species (including *K pneumoniae*), *Proteus mirabilis* and *Pseudomonas aeruginosa*

URINARY TRACT INFECTIONS (complicated and uncomplicated) caused by *E coli, Proteus mirabilis, Proteus vulgaris, M morganii* and *Klebsiella* species (including *K pneumoniae*)

UNCOMPLICATED GONORRHEA (cervical, urethral and rectal) caused by *Neisseria gonorrhoeae*, including both penicillinase and nonpenicillinase producing strains

PELVIC INFLAMMATORY DISEASE caused by *N gonorrhoeae*

BACTERIAL SEPTICEMIA caused by *Staph aureus, Strep pneumoniae, E coli, H influenzae* and *K pneumoniae*

BONE AND JOINT INFECTIONS caused by *Staph aureus, Strep pneumoniae, Streptococcus* species (excluding enterococci), *E coli, P mirabilis, K pneumoniae* and *Enterobacter* species

INTRA-ABDOMINAL INFECTIONS caused by *E coli* and *K pneumoniae*

MENINGITIS caused by *H influenzae, N meningitidis* and *Strep pneumoniae*. Ceftriaxone has also been used successfully in a limited number of cases of meningitis and shunt infections caused by *Staph epidermidis* and *E coli*.

PROPHYLAXIS: The administration of a single dose of ceftriaxone preoperatively may reduce the incidence of postoperative infections in patients undergoing coronary artery bypass surgery.

Although ceftriaxone has been shown to have been as effective as cefazolin in the prevention of infection following coronary artery bypass surgery, no placebo-controlled trials have been conducted to evaluate any cephalosporin antibiotic in the prevention of infection following coronary artery bypass surgery.

SUSCEPTIBILITY TESTING: Before instituting treatment with Rocephin, appropriate specimens should be obtained for isolation of the causative organism and for determination of its susceptibility to the drug. Therapy may be instituted prior to obtaining results of susceptibility testing.

CONTRAINDICATIONS: Rocephin is contraindicated in patients with known allergy to the cephalosporin class of antibiotics.

WARNINGS: BEFORE THERAPY WITH ROCEPHIN IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEPHALOSPORINS, PENICILLINS OR OTHER DRUGS. THIS PRODUCT SHOULD BE GIVEN CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS. ANTIBIOTICS SHOULD BE ADMINISTERED WITH CAUTION TO ANY PATIENT WHO HAS DEMONSTRATED SOME FORM OF ALLERGY, PARTICULARLY TO DRUGS. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE THE USE OF SUBCUTANEOUS EPINEPHRINE AND OTHER EMERGENCY MEASURES.

Pseudomembranous colitis has been reported with the use of cephalosporins (and other broad-spectrum antibiotics); therefore, it is important to consider its diagnosis in patients who develop diarrhea in association with antibiotic use.

ROCEPHIN® (ceftriaxone sodium/Roche)

Treatment with broad-spectrum antibiotics alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis. Cholestyramine and colestipol resins have been shown to bind to the toxin *in vitro*.

Mild cases of colitis respond to drug discontinuance alone. Moderate to severe cases should be managed with fluid, electrolyte and protein supplementation as indicated.

When the colitis is not relieved by drug discontinuance or when it is severe, oral vancomycin is the treatment of choice for antibiotic-associated pseudomembranous colitis produced by *C difficile*. Other causes of colitis should also be considered.

PRECAUTIONS: *GENERAL*: Although transient elevations of BUN and serum creatinine have been observed, at the recommended dosages, the nephrotoxic potential of Rocephin is similar to that of other cephalosporins.

Ceftriaxone is excreted via both biliary and renal excretion (see Clinical Pharmacology). Therefore, patients with renal failure normally require no adjustment in dosage when usual doses of Rocephin are administered, but concentrations of drug in the serum should be monitored periodically. If evidence of accumulation exists, dosage should be decreased accordingly.

Dosage adjustments should not be necessary in patients with hepatic dysfunction; however, in patients with both hepatic dysfunction and significant renal disease, Rocephin dosage should not exceed 2 gm daily without close monitoring of serum concentrations.

Alterations in prothrombin times have occurred rarely in patients treated with Rocephin. Patients with impaired vitamin K synthesis or low vitamin K stores (e.g., chronic hepatic disease and malnutrition) may require monitoring of prothrombin time during Rocephin treatment. Vitamin K administration (10 mg weekly) may be necessary if the prothrombin time is prolonged before or during therapy.

Prolonged use of Rocephin may result in overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Rocephin should be prescribed with caution in individuals with a history of gastrointestinal disease, especially colitis.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY: Carcinogenesis: Considering the maximum duration of treatment and the class of the compound, carcinogenicity studies with ceftriaxone in animals have not been performed. The maximum duration of animal toxicity studies was six months.

Mutagenesis: Genetic toxicology tests included the Ames test, a micronucleus test and a test for chromosomal aberrations in human lymphocytes cultured *in vitro* with ceftriaxone. Ceftriaxone showed no potential for mutagenic activity in these studies.

Impairment of Fertility: Ceftriaxone produced no impairment of fertility when given intravenously to rats at daily doses up to 586 mg/kg/day, approximately 20 times the recommended clinical dose of 2 gm/day.

PREGNANCY: Teratogenic Effects: Pregnancy Category B: Reproductive studies have been performed in mice and rats at doses up to 20 times the usual human dose and have no evidence of embryotoxicity, fetotoxicity or teratogenicity. In primates, no embryotoxicity or teratogenicity was demonstrated at a dose approximately three times the human dose.

There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproductive studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nonteratogenic Effects: In rats, in the Segment I (fertility and general reproduction) and Segment III (perinatal and postnatal) studies with intravenously administered ceftriaxone, no adverse effects were noted on various reproductive parameters during gestation and lactation, including postnatal growth, functional behavior and reproductive ability of the offspring, at doses of 586 mg/kg/day or less.

NURSING MOTHERS: Low concentrations of ceftriaxone are excreted in human milk. Caution should be exercised when Rocephin is administered to a nursing woman.

PEDIATRIC USE: Safety and effectiveness of Rocephin in neonates, infants and children have been established for the dosages described in the Dosage and Administration section.

ADVERSE REACTIONS: Rocephin is generally well tolerated. In clinical trials, the following adverse reactions, which were considered to be related to Rocephin therapy or of uncertain etiology, were observed:

LOCAL REACTIONS—pain, induration or tenderness at the site of injection (1%). Less frequently reported (less than 1%) was phlebitis after I.V. administration.

HYPERSENSITIVITY—rash (1.7%). Less frequently reported (less than 1%) were pruritus, fever or chills.

HEMATOLOGIC—eosinophilia (6%), thrombocytosis (5.1%) and leukopenia (2.1%). Less frequently reported (less than 1%) were anemia, neutropenia, lymphopenia, thrombocytopenia and prolongation of the prothrombin time.

GASTROINTESTINAL—diarrhea (2.7%). Less frequently reported (less than 1%) were nausea or vomiting and dysgeusia.

HEPATIC—elevations of SGOT (3.1%) or SGPT (3.3%). Less frequently reported (less than 1%) were elevations of alkaline phosphatase and bilirubin.

RENAL—elevations of the BUN (1.2%). Less frequently reported (less than 1%) were elevations of creatinine and the presence of casts in the urine.

CENTRAL NERVOUS SYSTEM—headache or dizziness were reported occasionally (less than 1%).

GENITOURINARY—moniliasis or vaginitis were reported occasionally (less than 1%).

MISCELLANEOUS—diaphoresis and flushing were reported occasionally (less than 1%).

Other rarely observed adverse reactions (less than 0.1%) include leukocytosis, lymphocytosis, monocytosis, basophilia, a decrease in the prothrombin time, jaundice, glycosuria, hematuria, bronchospasm, serum sickness, abdominal pain, colitis, flatulence, dyspepsia, palpitations and epistaxis.

DOSAGE AND ADMINISTRATION: Rocephin may be administered intravenously or intramuscularly. The usual adult daily dose is 1 to 2 gm given once a day (or in equally divided doses twice a day) depending on the type and severity of the infection. The total daily dose should not exceed 4 grams.

For the treatment of serious miscellaneous infections in children other than meningitis, the recommended total daily dose is 50 to 75 mg/kg (not to exceed 2 grams), given in divided doses every 12 hours. Generally, Rocephin therapy should be continued for at least two days after the signs and symptoms of infection have disappeared. The usual duration is 4 to 14 days; in complicated infections longer therapy may be required.

In the treatment of meningitis, a daily dose of 100 mg/kg (not to exceed 4 grams), given in divided doses every 12 hours, should be administered with or without a loading dose of 75 mg/kg.

For the treatment of uncomplicated gonococcal infections, a single intramuscular dose of 250 mg is recommended.

For preoperative use (surgical prophylaxis), a single dose of 1 gm administered ½ to 2 hours before surgery is recommended.

When treating infections caused by *Streptococcus pyogenes*, therapy should be continued for at least ten days.

No dosage adjustment is necessary for patients with impairment of renal or hepatic function; however, blood levels should be monitored in patients with severe renal impairment (e.g., dialysis patients) and in patients with both renal and hepatic dysfunctions.

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Vials containing 2 gm equivalent of ceftriaxone: Boxes of 10 (NDC 0004-1965-01)
Piggyback bottles containing 2 gm equivalent of ceftriaxone: Boxes of 10 (NDC 0004-1965-03)
Bulk pharmacy containers, containing 10 gm equivalent of ceftriaxone: Boxes of 1 (NDC 0004-1971-01)
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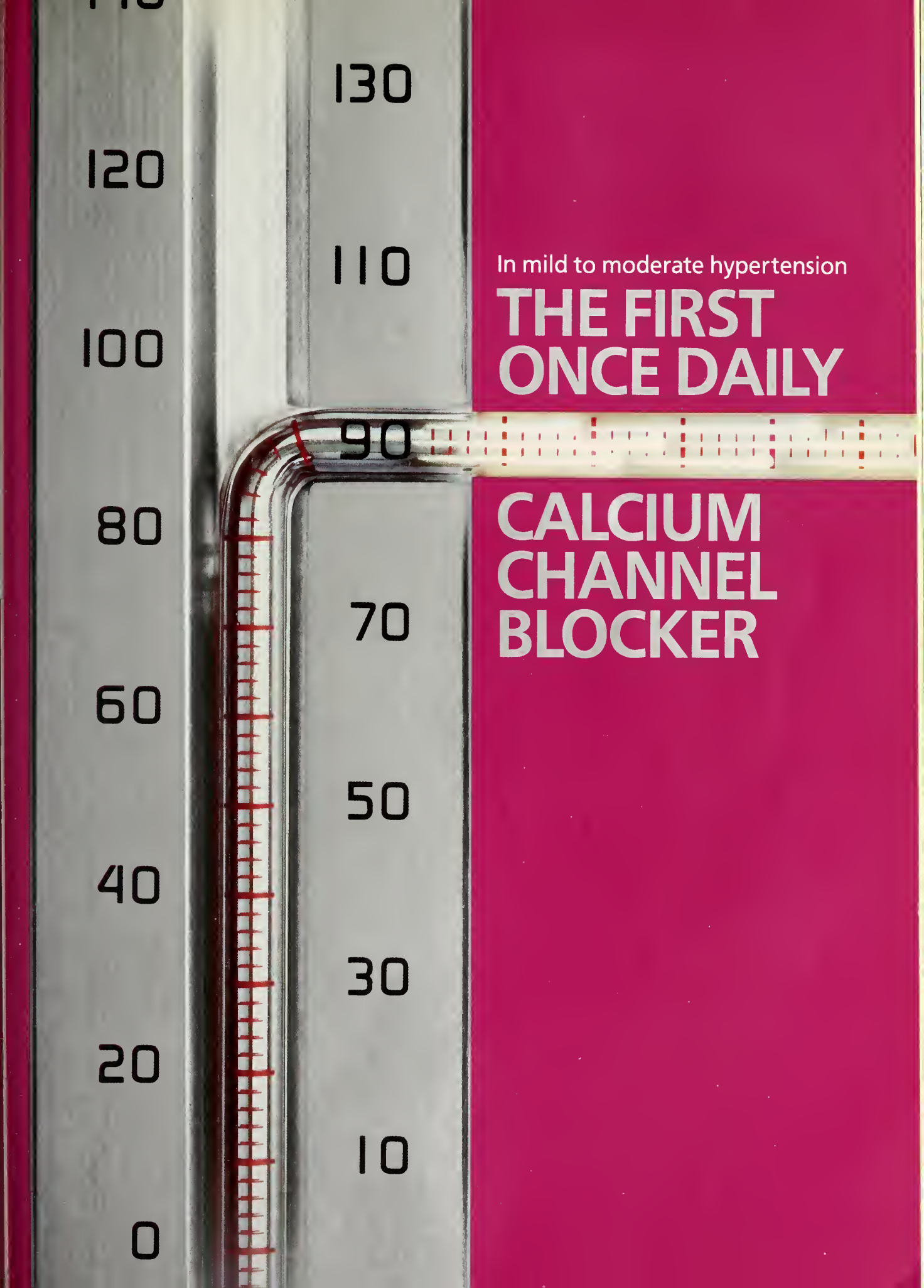
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References:

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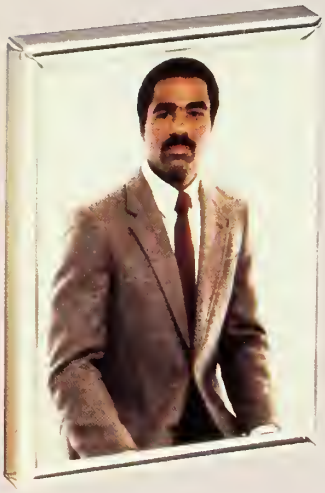
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JAMES B.
38, black male, heavy smoker. Prescribed a diuretic by another physician last year for hypertension.

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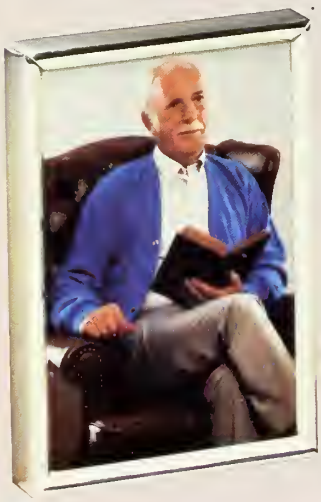
A LOGICAL CHOICE FOR CONTROL OF HIS BP
ISOPTIN* (verapamil HCl/Knoll) because...
— Black hypertensives often have low plasma renin activity and generally do not respond favorably to beta blockers.
— Beta blockers may increase the likelihood of bronchospasm.

ALICE W.
65, diabetic, overweight. Her BP has elevated to 190/98.

YOUR CONCERNS
She's on daily insulin.

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ISOPTIN* (verapamil HCl/Knoll) because...
— Unlike most beta blockers and diuretics, ISOPTIN has no adverse effects on serum glucose levels.
— Unlike most beta blockers, ISOPTIN does not mask the symptoms of hypoglycemia.





THOMAS G.
70, asthmatic. In the past, BP adequately controlled with 25 mg hydrochlorothiazide daily.

YOUR CONCERNS
Today patient presents with symptoms of gout. Workup reveals high uric acid level, low serum potassium, and BP elevated to 180/98.

A LOGICAL CHOICE FOR CONTROL OF HIS BP
ISOPTIN* (verapamil HCl/Knoll) because...
— Unlike diuretics, ISOPTIN will not decrease serum potassium levels or elevate uric acid levels.
— Unlike beta blockers, ISOPTIN can be used safely in asthma and COPD patients.

JOHN K.
42, Annual physical uncovered diastolic BP of 102... confirmed on three successive office visits. Unresponsive to nonpharmacologic intervention.

YOUR CONCERNS
Salesman, spends many hours of his working day in car... total cholesterol level 300, HDL 35.

A LOGICAL CHOICE FOR CONTROL OF HIS BP
ISOPTIN* (verapamil HCl/Knoll) because...
— Unlike diuretics, ISOPTIN does not cause urinary urgency.
— Unlike either beta blockers or diuretics, ISOPTIN will not adversely affect his already seriously compromised lipid profile.
— Unlike with propranolol, fatigue and impotence are rarely reported.



Antihypertensive therapy you and your patients can live with

Knoll Pharmaceuticals
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In mild to moderate hypertension
THE FIRST ONCE DAILY
CALCIUM CHANNEL BLOCKER

Brief Summary

ISOPTIN® SR
(verapamil HCl/Knoll)
240 mg scored, sustained-release tablets

CONTRAINDICATIONS: 1) Severe left ventricular dysfunction (see WARNINGS), 2) Hypotension (less than 90 mmHg systolic pressure) or cardiogenic shock, 3) Sick sinus syndrome or 2nd or 3rd degree AV block (except in patients with a functioning artificial ventricular pacemaker).

WARNINGS: **Heart Failure**: ISOPTIN should be avoided in patients with severe left ventricular dysfunction (see DRUG INTERACTIONS). Patients with milder ventricular dysfunction should, if possible, be controlled before verapamil treatment. Hypotension: ISOPTIN (verapamil HCl) may produce occasional symptomatic hypotension. Elevated Liver Enzymes: Elevations of transaminases with and without concomitant elevations in alkaline phosphatase and bilirubin have been reported. Periodic monitoring of liver function in patients receiving verapamil is therefore prudent. Accessory Bypass Tract (Wolff-Parkinson-White): Patients with paroxysmal and/or chronic atrial flutter or atrial fibrillation and a coexisting accessory AV pathway have developed increased antegrade conduction across the accessory pathway producing a very rapid ventricular response or ventricular fibrillation after receiving intravenous verapamil. While this has not been reported with oral verapamil, it should be considered a potential risk. Treatment is usually D.C.-cardioversion. Atrioventricular Block: The effect of verapamil on AV conduction and the SA node may cause asymptomatic 1st degree AV block and transient bradycardia. Higher degrees of AV block, while infrequent (0.8%), may require a reduction in dosage or, in rare instances, discontinuation of verapamil HCl. Patients with Hypertrophic Cardiomyopathy (IHSS): Although verapamil has been used in the therapy of patients with IHSS, severe cardiovascular decompensation and death have been noted in this patient population.

PRECAUTIONS: Impaired Hepatic or Renal Function: Verapamil is highly metabolized by the liver with about 70% of an administered dose excreted in the urine. In patients with impaired hepatic or renal function verapamil should be administered cautiously and the patients monitored for abnormal prolongation of the PR interval or other signs of excessive pharmacological effects (see OVERDOSAGE).

Drug Interactions: Beta Blockers: Concomitant use of ISOPTIN and oral beta-adrenergic blocking agents may be beneficial in certain patients with chronic stable angina or hypertension, but available information is not sufficient to predict with confidence the effects of concurrent treatment in patients with left ventricular dysfunction or cardiac conduction abnormalities. Digitalis: Clinical use of verapamil in digitalized patients has shown the combination to be well tolerated if digoxin doses are properly adjusted. However, chronic verapamil treatment increases serum digoxin levels by 50 to 75% during the first week of therapy and this can result in digitalis toxicity. Upon discontinuation of ISOPTIN (verapamil HCl), the patient should be reassessed to avoid underdigitalization. Antihypertensive Agents: Verapamil administered concomitantly with oral antihypertensive agents (e.g., vasodilators, angiotensin-converting enzyme inhibitors, diuretics, beta blockers, prazosin) will usually have an additive effect on lowering blood pressure. Patients receiving these combinations should be appropriately monitored. Disopyramide: Disopyramide should not be administered within 48 hours before or 24 hours after verapamil administration. Quinidine: In patients with hypertrophic cardiomyopathy (IHSS), concomitant use of verapamil and quinidine resulted in significant hypotension. There has been a report of increased quinidine levels during verapamil therapy. Nitrates: The pharmacologic profile of verapamil and nitrates as well as clinical experience suggest beneficial interactions. Cimetidine: Two clinical trials have shown a lack of significant verapamil interaction with cimetidine. A third study showed cimetidine reduced verapamil clearance and increased elimination to 1/2. Anesthetic Agents: Verapamil may potentiate the activity of neuromuscular blocking agents and inhalation anesthetics. Carbamazepine: Verapamil may increase carbamazepine concentrations during combined therapy. Rifampin: Therapy with rifampin may markedly reduce oral verapamil bioavailability. Lithium: Verapamil may lower lithium levels in patient on chronic oral lithium therapy. Carcinogenesis, Mutagenesis, Impairment of Fertility: There was no evidence of a carcinogenic potential of verapamil administered to rats for two years. Verapamil was not mutagenic in the Ames test. Studies in female rats did not show impaired fertility. Effects on male fertility have not been determined. Pregnancy (Category C): There are no adequate and well controlled studies in pregnant women. ISOPTIN crosses the placental barrier and can be detected in umbilical vein blood at delivery. This drug should be used during pregnancy, labor, and delivery, only if clearly needed. Nursing Mothers: ISOPTIN is excreted in human milk, therefore, nursing should be discontinued while verapamil is administered. Pediatric Use: Safety and efficacy of ISOPTIN in children below the age of 18 years have not been established.

ADVERSE REACTIONS: Constipation 8.4%, dizziness 3.5%, nausea 2.7%, hypotension 2.5%, edema 2.1%, headache 1.9%, CHF/pulmonary edema 1.8%, fatigue 1.7%, bradycardia 1.4%, 3° AV block 0.8%, flushing 0.1%, elevated liver enzymes (see WARNINGS). The following reactions, reported in less than 1.0% of patients, occurred under conditions (open trials, marketing experience) where a causal relationship is uncertain; they are mentioned to alert the physician to a possible relationship: angina pectoris, arthralgia and rash, AV block, blurred vision, cerebrovascular accident, chest pain, claudication, confusion, diarrhea, dry mouth, dyspnea, ecchymosis or bruising, equilibrium disorders, exanthema, gastrointestinal distress, gingival hyperplasia, gynecomastia, hair loss, hyperkeratosis, impotence, increased urination, insomnia, macules, muscle cramps, myocardial infarction, palpitations, paresthesia, psychotic symptoms, purpura (vasculitis), shakiness, somnolence, spotty menstruation, sweating, syncope, urticaria. Treatment of Acute Cardiovascular Adverse Reactions: Whenever severe hypotension or complete AV block occur following oral administration of verapamil, the appropriate emergency measures should be applied immediately, e.g., intravenously administered isoproterenol HCl, levarterenol bitartrate, atropine (all in the usual doses), or calcium gluconate (10% solution). If further support is necessary, inotropic agents (dopamine or dobutamine) may be administered. Actual treatment and dosage should depend on the severity and the clinical situation and the judgment and experience of the treating physician.

OVERDOSAGE: Treatment of overdosage should be supportive. Beta-adrenergic stimulation or parenteral administration of calcium solutions may increase calcium ion flux across the slow channel, and have been used effectively in treatment of deliberate overdosage with verapamil. Clinically significant hypotensive reactions or fixed high degree AV block should be treated with vasopressor agents or cardiac pacing, respectively. Asystole should be handled by the usual measures including cardiopulmonary resuscitation.

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Over the last 40 years, research programs supported by the American Cancer Society have made increasing progress in the treatment, detection and prevention of cancer.

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Which is why, this year, hundreds of thousands of people will be successfully treated for the disease.

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Help us keep winning.

The Complete Physician: Is the Goal Worth Striving for?

Reflections of an 88-Year-Old Physician

PAUL S. RHOADS, M.D.
Richmond

CONSIDERING THE great number of paths which a medical career may take, there can never be a consensus on exactly what the term "complete physician" means. To me it means uncompromising dedication to the needs of the individuals our profession serves, in any way that our talents can be used. Once having acquired the fundamentals, the young physician can choose to serve through one of many channels—direct care of patients, public health, foreign mission medical work, teaching, research, etc. The variety of choices is almost endless.

For nearly three-quarters of a century I have been engaged in various aspects of medicine—private and consulting practice; teaching; research; administration; editing of a major journal (*AMA Archives of Internal Medicine*); and travel. Among my travels were five trips of several weeks each to survey Christian mission medical schools and hospitals in India, Korea and Lebanon for comparison with the medical institutions of the respective countries. At my advanced age I still have convictions concerning what a complete physician should be and am aware that no one can actually attain that goal. The journey in pursuit of the goal has, for me, always been exciting and rewarding.

Most of the members of my class of 1920 had just been discharged from the armed forces following World War I when we entered medical school; and we were told, as hundreds of medical school classes have been told, that physicians have three primary obligations: (1) to care for patients, using all the means at our disposal to cure and prevent disease; (2) to teach our art to others; and (3) to add whatever possible to the sum total of medical knowledge. The various ways in which this three-pronged responsibility might be achieved became apparent as the months of training went on—ways as different as the personal attitudes of the students and physicians involved. The common denominator was the fact that no matter what route was chosen, our business was and is with human lives. This responsibility should be the dominant driving force for all physicians in the pursuit of their careers.

We are now at a time when the physician's role as perceived by both the public and himself is changing. Dr. Arnold S. Relman, distinguished editor

About the Author

Dr. Paul S. Rhoads, 88, professor emeritus of medicine, Northwestern University School of Medicine, Evanston, Ill., died Jan. 24. At the age of 73, after 47 years of practice, he moved from Chicago to Richmond, Ind., where he was appointed director of medical education at Reid Memorial Hospital. He held the position until last year.

Dr. Rhoads was a 1925 graduate of Rush Medical College, Chicago. He was a former chief of the Department of Medicine at Chicago Wesley Memorial Hospital.

He was a former editor of the *Archives of Internal Medicine* and, as an author, had contributed numerous scientific reports to the medical literature, most of which focused on infectious diseases.

Dr. Rhoads had been active in an editorial capacity for INDIANA MEDICINE since 1973 when he was elected to the Editorial Board; for the past two years he had served as a consulting editor.



Doctor Rhoads

of *The New England Journal of Medicine*, has eloquently expressed many of the reasons for this change.[1] He says the collective behavior of physicians has deteriorated. They no longer are automatically subordinating their own interests to those of the society they serve. Developments that are disturbing to all of us include the rapid heretofore unrestricted proliferation of third party payment for health care of all sorts. This has encouraged a laxness in keeping down expenses of patient care; high cost medical technology has risen at an amazing pace. Examples include: open heart surgery; organ transplants; laser beam diagnosis and surgery; sophisticated diagnostic procedures such as CT scans, molecular resonance testing, organ imaging and the like. (One had better have insurance!) There is a surfeit of specialists who work with these technologies and often set their fees commensurate with the excessive cost of the equipment required for the new techniques.

Among the most pernicious of the changes in provision of care is the growing concept that it can be obtained at a price like any other commodity regardless of the dedication and moral commitment of those who supervise

Dr. Paul Rhoads Was a Physician's Physician

Four days after Dr. Rhoads' death Jan. 24, 1987, the following article appeared as a "Guest Opinion" in the *Richmond Palladium-Item*. It was written by C. Edward Kaeuper, a retired *Palladium-Item* editor and columnist. The article is reprinted with permission.

Death has now kept Dr. Paul S. Rhoads from seeing in print one of the last things he had written, an article entitled, "The Complete Physician." Yet he did have the pleasure of knowing that it had been accepted for publication by INDIANA MEDICINE.

Dr. Rhoads told me about that article during a visit at his home a few months ago. It was just recently that it had been completed and Mrs. Rhoads said he was pleased to learn that it had been accepted.

Over the years he had published over a hundred medical papers and for 10 years was chief editor of *Archives of Internal Medicine* for the American Medical Association.

Yet his version of "The Complete Physician," which will draw upon years of personal experience—for treating a patient to him was always paramount—no doubt will be of keen interest to the medical profession. In a life devoted to medicine, he always said without hesitation that "taking care of patients" gave him the most satisfaction.

He always said early retirement was not for him. That accounted for his service to Reid Memorial Hospital as director of medical education until ill health confined him to his home. Even then, as long as he could, he continued to serve the hospital's medical education effort in a consulting capacity.

Dr. Rhoads said that if persons in later life want to take a different direction and develop new interests, "that would be great just as long as they didn't sit on their bottoms."

His home is along Beeson Road south of the city where, while his health permitted, he enjoyed a vegetable garden. But, as he said, "the woods, wild flowers and stream are mostly just to enjoy."

Many persons, especially fellow physicians, remember him, too, as an ardent sports fan. He was watching one game on television and had a radio tuned to another when I stopped by one Saturday afternoon last fall.

Just a little over a week before he died, Dr. Paul Runge was a visitor and together they watched some sports events on television. He especially was interested in Indiana and Purdue teams and was able, despite his illness, to see Purdue lose a close basketball game to Iowa. When Indiana played Iowa a few days later, he wasn't up to watching, Dr. Runge said.

Dr. Rhoads always remembered with a laugh a meeting he had arranged in Chicago but for which he had forgotten to line up an opening prayer. So the task fell to him. For some reason, he remembered, instead of saying "Amen," he said "Truly yours, Paul S. Rhoads."

On another occasion, though, Dr. Rhoads remembered, he was quite prepared for the invocation and did what he felt would have done credit to a minister. Bob Hope, one of the speakers, turned to him and said:

"What's the matter, Doc? Business getting bad and you're doing a little moonlighting?"

Dr. Rhoads maintained his sense of humor. He liked to laugh with people, not at them, yet he never hesitated to tell stories on himself.

His death at 88 makes his article, "The Complete Physician," of potentially greater interest. Even though he'll not now see it in print, he had the satisfaction of knowing that many others will. A circulation area wider than that of INDIANA MEDICINE is appropriate.

and deliver it. The burgeoning of for-profit hospitals and clinics throughout the whole nation is a shining example.

Few of us would have the clock turned back, even if that were possible. The tremendous advances in curative and preventive medicine are almost unbelievable. At the turn of the century the average age of death was in the 40s. With the arrival of new treatment modalities, including antibiotics, the average age of death is now in the low 70s. Yet the older generation of patients is keenly aware that something just as important as pills and skills and sophisticated technology is missing. The older doctors, too, are aware of a certain deficiency. Much of the joy and personal satisfaction derived from their efforts is gone. The younger patients no longer see the physician as a reliable friend, interested in all the circumstances which make them physically or emotionally sick. Too often they feel that physicians have lost respect for their personal identity while retaining an interest in their ability to pay the fees. Also, because of new medical knowledge with which all of us are bombarded by television and the news media, they quickly learn that many physicians are not keeping up with the changing scene in medicine. The public is aware that something has gone awry, though they do not know what it is.

The public does not expect doctors to be infallible. They do expect them to be competent and understanding. Patients want their doctors to talk to them. Based upon my considerable experience with teaching hospitals as a faculty member, practicing physician, and as a patient, I know that by and large, history-taking and physical examinations are not done as thoroughly as in days gone by.

In teaching undergraduates, I formed the habit of asking patients on services other than my own, with the consent of their physicians, to let my group of students and hospital residents question and examine them, at the same time withholding access to the patients' charts. Subsequently, inside a closed conference room, we discussed the probable diagnosis, what further work-up was needed, and how the patient should be treated. Although I have no "hard data" to back me up, I feel sure that three-fourths of the diagnoses could have been made by simply talking to and examining the patient, appropriate confirmation being obtained by *routine* laboratory tests. Quite often key points in the history and physical examination were important enough to be transmitted to the patient's regular physician if one sensed that he might welcome them and not be embarrassed.

In quizzing students and residents, I have been astonished by the casualness with which CT scans, sonograms, and also many potentially dangerous invasive tests are suggested by our young colleagues when they clearly are not needed. Also, one is impressed by the number of consultants called in to make decisions because of the primary physician's lack of confidence or fear of malpractice suits. Some consultants fail to take the trouble to learn what has already been established by previous examiners. Understandably, the bewildered patient concludes that he is being cared for by a committee, the chairman of which is uncertain, if, indeed, one exists at all.

'You Will Be Rewarded by the Esteem and Respect of Your Patients if You Earn It'

House calls are also becoming obsolete. Many of our young physicians absolutely refuse to make them. If they knew how much could be learned about a patient in his or her homesetting and what a morale builder a physician's visit might be, perhaps they would not be so adamant in their refusal to visit patients who are unable to get to them. What patients are missing is the physician's understanding and genuine caring about their problems, physical or emotional, imagined or real. They need a doctor who is also a friend.

In spite of some of the undesirable developments described above, we must admit that there were some unscrupulous doctors practicing earlier in this century, just as there are now. The present generation of physicians, for the most part, enter their profession with high ideals. My personal view, however, is that more of them are allowing these ideals to deteriorate than in the past; and I fear that greed is the chief malefactor.

Turning to the positive side, it should be noted that more care is being given to the selection of students for entrance to medical school. One is impressed by the character and intelligence of the majority of the young people entering our profession. They have a staggering amount of medical knowledge and technology to learn. Fortunately, they have available as helpers in their care of patients superbly trained nurses, paramedics, and technicians with whom they can work comfortably. Continuing medical education and peer review as essential to the physician's professional career is receiving more emphasis.

My personal involvement with continuing education came about when, at age 73, for family reasons, my wife and I moved to Richmond, Indiana (pop. 46,000). I was asked to be director of the CME program at Reid Memorial, a good community hospital of 350 beds. The program, started a few months before my arrival, was interrupted by the sudden death of the physician designated to get it under way. A new

start had to be made. This man's widow gave $10,000 for a medical library for the hospital. Expansion of the hospital building had begun. The Board of Trustees was persuaded to include in its plans an auditorium seating 210 people and space for a larger library.

During the following 15-year period, the library expanded to approximately 800 volumes of new textbooks, and the number of journal subscriptions rose from five to 50 or more. Medical conferences for the entire professional staff were conducted at 7:30 a.m. every Wednesday and Saturday. They were given over to Grand Rounds, case reports, death conferences, and presentations by faculty members from the nearest medical schools. This program was financed by a small grant from the state which was slightly over-matched by the hospital itself.

We were also able to conduct four all-day seminars every year in which three or four speakers from Indiana University School of Medicine were included. The rest were recruited from leading schools of the midwest and the eastern seaboard. Though they were paid little more than travel expenses, well known faculty members, many of them department heads, eagerly accepted our invitations. These all-day conferences, paid for by the attendees, were as high in quality as those put on by leading medical schools. As predicted, a certain portion of the physician staff did not take advantage of the programs offered, but those who did profited immensely. Good teaching talent surfaced among our staff. Some clinical research resulted, chiefly reports of unusual cases with short reviews of the subject illustrated; and a few well planned studies in our clinical laboratory were published.

Beyond the positive developments in continuing medical education, one senses the growing emphasis by many leading medical schools on the humanities—history, literature, sociology, music and the like—in pre-medical studies.[2] In some instances, such studies are carried over to medical school itself. In other words, efforts are surely under way to turn out more complete physicians. The three-legged stool of caring for patients; teaching colleagues, students, and patients; and adding to the bulk of medical knowledge and skill is still flourishing. The old Peabody axiom of the secret of *caring* for the patient as the *sine qua non* of good medical care is still in vogue.

These days, however, practicing physicians sense little or no possibility of participation in complicated research. The bulk of our highly sophisticated technological research must, of course, be performed by those specially trained for it. Physicians dealing directly with patients supply the demand for the efforts of the full time researchers.

We must remember that at the turn of the century and for several years afterward, tremendous strides were made in medical knowledge by researchers who had no laboratories beyond those of the hospitals or agencies in which they worked. Most research was done at their own expense. The work of Dr. James B. Herrick on the description of sickle cell anemia and of the clinical manifestations of coronary artery disease,[3] and the discovery of the cause of scarlet fever by Drs. George and Gladys Dick[4] are examples which I know of at first hand.

My own more modest research efforts dealt with normal and abnormal bacterial content of various parts of the body, the effect of two or more infections occurring simultaneously, control of hemolytic streptococcus infections and the like. Reports on more than 50 of these studies were published in appropriate medical journals.

Before I leave the topic of full time teachers and researchers, let me assure you that a great many of them share as much concern for a given patient's welfare as the practicing physicians who look after their patients on a day-to-day basis. In ward rounds or outpatient clinics the attitude of the full time teachers rubs off on those they are teaching even though their contact with patients is minimal. They understand as well as the practitioners the importance of creating an atmosphere of "We are in this thing together, and we'll help all we can—" from which students, residents, and nurses take their cue.

'Those Who Teach Must Stress Continually the Old Ideals of the Medical Profession'

I am convinced that most medical students enter the field because they see in it an opportunity to improve the lot of their fellow human beings. Some have other goals: to be assured a good income, a position of respect in the community, an opportunity to pursue "bench work" in the laboratories, etc. It is the obligation of those who teach them to stress continually the old ideals of the medical profession. Many medical schools are adding courses in ethics to their already crowded curricula.

In my own view, how best to live with and improve the world is learned in family, religious, and school life—and through contact with our peers. For me, bedside teaching has been more important than lectures, though of the latter I have performed my share. In later years I made a point of holding one special session with each of the various groups assigned to me in which we talked over personal motivations and goals. Unashamedly, because of my white hair and deeply held convictions, I gave each of them

a typed page inscribed with the following precepts:

- Study consistently; learn principles and processes. Facts and figures can always be looked up. You must have hard-nosed competence in the practice of your profession.
- Work out a routine of study hours and study habits. Keep in mind that the need to study will never end.
- Work out your own reference file and stick to it through all your years of preparation.
- When you begin to have contact with patients, try always to put yourself in the patient's place. Courtesy, kindness, and honesty must be your watchwords. Learn patience. Listen. Ask the right questions. Be thorough in your examination.
- Be patient and thorough in your preparation; your whole medical life depends upon the quality of your preparation.
- When a particular facet of medicine excites your interest, pursue it. Try to accomplish at least one good research project before you finish your residency. Go on with a fellowship if you can possibly afford the time and money.
- Above all, never let financial considerations affect your judgment in the choice or location of your career. You can always make a living. *All* the other considerations are more important.
- Remember that you are highly privileged to be in the position of serving your fellow men in their times of greatest need. Never regard that privilege lightly. You will be rewarded by the esteem and respect of your patients and your community *if you earn it.*

Usually I have added the following advice for doctors quoted from the litany prepared by Sir Robert Hutchinson, a wise old physician of London:

"From inability to let well alone; from too much zeal for the new and contempt for what is old; from putting knowledge before wisdom, science before art, and cleverness before common sense, from treating patients as cases, and from making the cure of the disease more grievous than the endurance of the same, Good Lord deliver us."

In closing, I refer to my original thesis. There will never be a *complete* physician. However, the striving for learning more of what our profession may now do for our patients, though more difficult than in the past, makes it all worthwhile. If we return to our old ideals of doing all we can for those we serve in curative and preventive medicine, and in spiritual support, the future indeed appears bright.

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Look-Alike and Sound-Alike Drug Names

BENJAMIN TEPLITSKY, R. PH.
Brooklyn, N.Y.

Look-alike and sound-alike drug names can be misinterpreted by a nurse reading doctors' orders or by a pharmacist compounding physicians' prescriptions. Such misunderstandings can result in the administration of a drug not intended by the prescriber. Awareness of such look-alike and sound-alike drug names can reduce potential errors.

	VERSED	VEPESID
Category:	Sedative & Hypnotic	Mitotic inhibitor
Brand Name:	Versed, Roche	VePesid, Bristol
Generic Name:	Midazolam HCl	Etoposide
Dosage Forms:	Injection	Injection

	AMRINONE	AMIODARONE
Category:	Cardiac agent	Arrhythmic
Brand Name:	Inocor, Winthrop-Breon	Cordarone, Wyeth
Generic Name:	Amrinone Lactate	Amiodarone
Dosage Forms:	Injection	Tablets

CME QUIZ

TO OBTAIN ONE HOUR OF CATEGORY 1 AMA CME CREDIT, answer the following questions by circling the correct answer on the answer sheet below. Complete and clip the application form and mail it to: Indiana University School of Medicine, CME Division, BR 156, 1226 W. Michigan St., Indianapolis 46223.

Myasthenia Gravis

CONTINUED FROM PAGES 215-222

1. First step for treatment of patients with MG is:
   a. Performed thymectomy
   b. Begin with corticosteroids
   c. Use of anticholinesterase
   d. None of the above.
2. Anticholinesterase agents:
   a. Are useful in all types of myasthenia
   b. Are the most effective drugs in treating MG
   c. Act on all skeletal muscles to the same degree
   d. Do not show inter-individual variability
3. In patients who are on anticholesterase, use of atropine:
   a. Is justified routinely
   b. Usually is administered if the patient develops muscarinic side effects
   c. May be used routinely with caution
   d. Is only indicated if muscarinic side effects are serious
   e. Should be individualized
4. Corticosteroids:
   a. Produce moderate to marked improvement in the majority of patients with MG
   b. Young myasthenic patients usually respond better than elderly
   c. Response is unpredictable
   d. Response usually takes 1-2 weeks to achieve a steady response
5. The major drawback of corticosteroid use is its:
   a. Expense
   b. Unpredictable response
   c. Undesirable long-term side effects.
   d. Fluctuation of myasthenia during reduction of dose.
6. Use of immunosuppressive drugs prior to thymectomy:
   a. Is mandatory
   b. Is thought to decrease the morbidity and mortality of the procedure
   c. Increases the percentage of remission.
   d. May reduce the size of the thymus gland
7. Azathioprine:
   a. Is indicated in all patients with MG
   b. Produces remission in 40-50% of the cases
   c. The average time response is about 12 months
   d. Is the first line drug for patients with generalized MG
8. Plasmaphoresis:
   a. Produces permanent improvement in myasthenic patients
   b. Is the best approach for patients undergoing thymectomy
   c. Is a most effective and reliable procedure for myasthenic crisis
   d. Its effect usually occurs following the first exchange
   e. None of the above
9. During pregnancy:
   a. Myasthenia usually exacerbates
   b. If necessary, thymectomy should be performed
   c. Prednisone and Mestinon doses should be increased
   d. Patients should be hospitalized at least one week before delivery
   e. Treatment is essentially the same as in a non-pregnant woman, but the mother and fetus should be closely monitored.
10. Treatment of crisis includes all of the following except for:
    a. Securing airway
    b. Discontinuing Prednisone and Mestinon
    c. Discontinuing Mestinon
    d. Identifying and treating the precipitating cause
    e. If necessary, plasma exchange

JANUARY CME QUIZ Answers

Following are the answers to the CME quiz that appeared in the January 1987 issue: "Fluid and Electrolyte Disturbances in the Perioperative Period," by Craig M. Stoops, M.D.

1. c	6. a
2. c	7. b
3. d	8. b
4. b	9. e
5. c	

Answer sheet for Quiz: (Myasthenia Gravis)

1. a b c d	6. a b c d
2. a b c d	7. a b c d
3. a b c d e	8. a b c d e
4. a b c d	9. a b c d e
5. a b c d	10. a b c d e

I wish to apply for one hour of category 1 AMA Continuing Medical Education credit through the I.U. School of Medicine. I have read the article and answered the quiz on the answer sheet above. I understand that my answer sheet will be graded confidentially, at no cost to me, and that notification of my successful completion of the quiz (80% of the questions answered correctly) will be directed to me for my application for the Physician's Recognition Award of the American Medical Association. I also understand that if I do not answer 80% of the questions correctly, I will not be advised of my score but the answers will be published in the next issue of INDIANA MEDICINE.

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AUXILIARY REPORT

Alfrieda Mackel (Mrs. Frederick)
ISMA Auxiliary President 1986-87

AGENDA
43RD ANNUAL HOUSE OF DELEGATES
INDIANA STATE MEDICAL ASSOCIATION
AUXILIARY

APRIL 28, 29 and 30, 1987
FORT WAYNE MARIOTT INN
305 East Washington Center Road
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TUESDAY, APRIL 28, 1987

10:00 a.m. to 5:00 p.m. ..... Registration
10:00 a.m. ..... Finance Committee Meeting
11:00 a.m. ..... Executive Committee Meeting
12:30 p.m. ..... Joint Board Luncheon—Outgoing & Incoming
1:30 p.m. ..... Pre-Convention Board Meeting
3:00 p.m. ..... New 1987-88 Board Meeting
4:00 p.m. ..... Past Presidents Meeting
6:00 p.m. ..... Candlelight Dinner at the Foellinger & Freimann Botanical Conservatory, catered by the award-winning Cafe Johnell, honoring ISMA-A Past-Presidents. Entertainment.

WEDNESDAY, APRIL 29, 1987

7:30 a.m. to 5:00 p.m. ..... Registration
7:30 a.m. to 8:30 a.m. ..... Hot Breakfast Buffet
8:45 a.m. ..... Formal Opening, House of Delegates Meeting
9:00 a.m. ..... Memorial Service
Business of the House of Delegates
Central & Southern Area Reports
12:00 noon ..... Recess
12:30 p.m. ..... Luncheon, Style Show
2:00 p.m. to 3:30 p.m. ..... Panel Discussion: "The Impaired Physician & the Family"
6:30 p.m. ..... Reception—Cash Bar
7:30 p.m. ..... Dinner, Marriott Ballroom
Entertainment by "Quintessance"
Spouses Welcome

THURSDAY, APRIL 30, 1987

7:30 a.m. to 11:30 a.m. ..... Registration
7:30 a.m. to 8:30 a.m. ..... Hot Breakfast Buffet
8:45 a.m. ..... House of Delegates Reconvenes
9:00 a.m. ..... Keynote address: Mrs. Edward Szewczyke (Betty) President-Elect, AMA-Auxiliary
Business of the House of Delegates
Northern Area Reports
11:45 a.m. ..... Invitation for 1988 House of Delegates Meeting
12:00 noon ..... Recess
12:30 p.m. ..... Photographs: Incoming-Outgoing Boards
1:00 p.m. ..... Luncheon and Installation Ceremony
Adjournment of the House of Delegates

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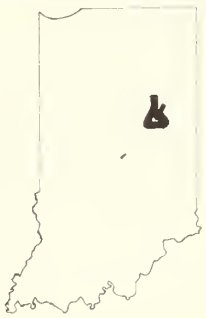
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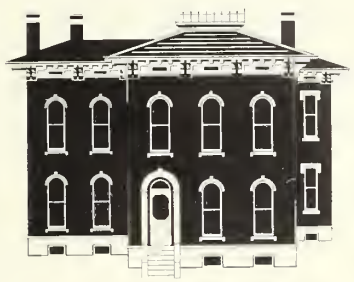
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For the Asking

• The Indiana Center for Surgery and Rehabilitation of the Hand conducts monthly conferences for the continuing education of those interested in hand surgery. For information about the schedule and subjects, contact Beth Bush, Conference Coordinator, P.O. Box 80434, 8501 Harcourt Road, Indianapolis 46280—(317) 875-9103.

• "A Look at Child Abuse" is the subject of a 45-page booklet written by Jon R. Conte, Ph.D., associate professor at the University of Chicago. The booklet was published by the National Committee for Prevention of Child Abuse because of the widespread lack of knowledge among the public in regard to the subject. To order, contact NCPCA at 332 S. Michigan Ave., Suite 950, Chicago 60604—(312) 663-3520.

• "Preventing AIDS . . . A Practical Guide for Everyone" is an 85-page single-source, comprehensive text for minimizing the risk of transmission or contraction of the AIDS virus. Specific and general preventive measures are given for the general public, high risk persons, and for those engaged in health care, personal service, food service and child care. The contents are based on U.S. government research reports. $9.95 per copy plus $2 for shipping and handling. Write JALSCO Inc., P.O. Box 30226, Cincinnati, Ohio 45230.



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• The National Commission on Correctional Health Care has completed its revision of publications that set national standards for correctional health care. The standards were originally developed by the AMA in the mid-1970s and, since 1982, have been used by the National Commission in its program to improve medical care and health services in the nation's jails and prisons. $15 per copy. Contact the Commission at Box 3500, 2000 Racine, Chicago 61614—(312) 528-0818.

• "Cancer Screening: What You Can Do to Detect Cancer" is a 26-page booklet published by the American Council on Science and Health. It emphasizes that, with the proper screening tests to detect the three major forms of cancer in a very early stage, and with the proper treatment, the cure rate for the three major malignancies can be raised to almost 100%. These include cancers of the uterine cervix, the breast and colon. The booklet should be standard reading material in physicians' offices, should be a reference source for the news media, and should be the foundation for all public education projects. For a copy, send a SASE (66¢, #10) to Cancer Screening Report, ACSH, 47 Maple St., Summit, N.J. 07901. Multiple copies are always available from the ACSH.

How Harmful Is Dioxin?

Experts who have worked a long time to dispose of dioxin say there is still no hard proof that dioxin is harmful to human health, according to "The Dioxin Paradox," an article that appears in the February issue of *Civil Engineering.*

So far, no one from Quail Run mobile home park, one of the residential areas in Missouri hit hardest by dioxin contamination in 1971, has died because of dioxin exposure. Residents also report no greater incidence of clinical illness than those people who were not exposed. Periodic check-ups showed only some non-specific changes in liver enzymes, which could be found in anyone, and some immune function changes.

Birth Problems Registry Now a Reality in Indiana

As required by Indiana Code 16-4-10, which went into effect Jan. 1, the State Board of Health has established a Birth Problems Registry to record all Indiana cases of birth problems—birth defects, stillbirths and low birth weight.

All cases of birth problems now must be reported by physicians, nurse midwives and hospitals. This is to be done by completing an Indiana Live Birth Certificate Supplemental Form, now being distributed to hospital administrators and medical records staffs.

By January 1988, when the National Center for Health Statistics revises the national birth certificate, the supplemental information will be incorporated into the birth certificate. At that time, only one form, the revised Live Birth Certificate, will be required.

National Eye Care Project Helps 2,000 Older Hoosiers

The American Academy of Ophthalmology announces that volunteer Indiana ophthalmologists have uncovered 289 cases of cataracts, 27 cases of glaucoma, 62 cases of macular degeneration and 12 cases of diabetic retinopathy among elderly Indiana residents who have called the toll-free Helpline—1-800-222-EYES (3937)—to receive assistance through the National Eye Care Project conducted by the Academy.

A total of 2,030 calls on the Indiana Helpline resulted in the discovery of the above cases. This public service, which offers medical eye care to the disadvantaged elderly at no out-of-pocket cost, is possible because of joint sponsorship by the Indiana Academy of Ophthalmology and the Foundation of the American Academy. It is available to U.S. citizens or legal residents, age 65 or over, who are not currently under the care of an ophthalmologist and who have not seen one within the past three years.

Ground Broken for New Health Education Center

Ground was broken in March for the new $4 million Life/Leadership Health Education Center in Indianapolis. The facility, which should be completed in a year, is located at 1900 N. Capitol Ave. on land provided by Methodist Hospital of Indiana.

One of the Center's supporters, Dr. H. Dean Evans, declares, "Schools cannot adequately address health problems in a vacuum. We need the effort of the home, the school, and the community."

The new building, financed by a public Capital Campaign Fund, will provide an extension of the health curriculum of public schools. It is expected to attract 100,000 kindergarten through 12th grade students annually from central and southern Indiana schools.

The Center's focus will be on PREVENTION, and programs will promote positive lifestyles.

The Center will contain about 25,000 square feet and will include eight teaching theaters, an exhibit hall featuring hands-on exhibits, an auditorium and several classroom/conference areas.

Marion Surgeon Attacks Smoking, Drinking

Dr. S. Gopal Raju, a Marion general surgeon, is vehement in his opposition to drugs, drunk driving, smoking and chewing tobacco. In fact, he has mounted a one-man campaign to publicize his convictions.

In Marion, Dr. Raju promotes his cause in print and during appearances on a local television station every other Thursday. He says Americans spend $50 billion on tobacco products and $120 billion on illegal drugs every year. In addition, he says they drink 600 billion gallons of beer and a billion gallons of wine and liquor every year.

Since he began his campaign, Dr. Raju has convinced about 30 of his patients to quit smoking; this year he wants to persuade 70 more to quit; toward this end, he has started a free Quit Smoking Club, which meets for an hour every Thursday.

Dr. Raju takes advantage of every opportunity to promote his messages. Last fall, for example, he supported the Great American Smokeout and, during a visit to India, used some of his time to address these issues in Bangalore and Anekal.

Host Families Wanted for Exchange Students

Host families are being sought for 25 high school students from Sweden, Norway, Denmark, Finland, Holland, Belgium, Austria, Switzerland, Germany, Spain, France, Italy, Ecuador, Australia and Japan for the 1987-88 school year in a program sponsored by the American Intercultural Student Exchange (AISE).

The students, age 15 through 17, will arrive in the U.S. in August 1987, attend local high schools, and return to their homes in June 1988. They are fluent in English, have been screened by school representatives in their home countries, and have spending money and medical insurance.

AISE is also seeking American high school students, age 15 through 17, who would like to spend a high school year in Sweden, Norway, Denmark, Germany, Switzerland, France, Spain or Australia or participate in a five-week summer host family stay throughout Western Europe.

Families interested in this program should call toll free 1-800-SIBLING (742-5464).

Terre Haute Newspaper Profiles Dugger Physicians

Doctors Joseph and Betty Dukes, long-time husband-wife family physicians in Dugger, were the subjects of a full-page photo feature in a December Sunday edition of *The Tribune-Star*, a Terre Haute daily newspaper.

The Dukes—"Doctor Joe" and "Doctor Betty" as Sullivan County people refer to them—have been practicing in Dugger since 1947. She enjoys obstetrics and has delivered more than 10,000 babies. Doctor Joe prefers radiology and cardiology. "But both doctors swear their allegiance is to family practice," *Tribune-Star* reporter Marilyn Salesman wrote.

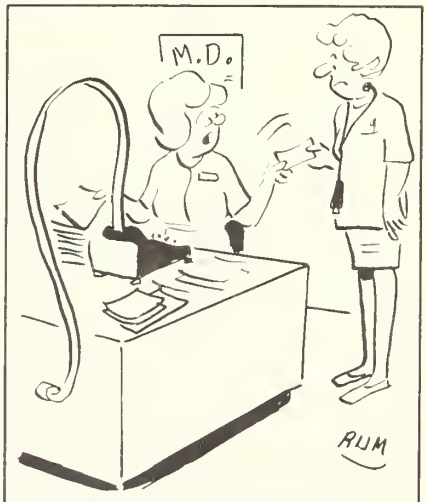
Both physicians, who are I.U. School of Medicine graduates, are in their mid-Sixties now but they continue to be in their office at least six days a week. In addition, Doctor Joe, a past ISMA president, finds time for banking and politics. He helped start a bank in Sullivan and is still on its board of directors; he is also active and well known in political circles.

Doctor Joe's father was a physician and today two of their three sons are physicians.

Koala Center Offers Older Adults Program

The Koala Center at Lebanon has begun an "Older Adults Treatment Program." Patients over 60 years old present special issues to be addressed as part of their treatment and recovery process. The "Older Adults Program" is characterized by strong emphasis on individualized treatment planning and treatment components.

Koala Centers operate inpatient and outpatient alcoholism and drug abuse treatment facilities in nine states.



"Here's the tape on income—I'm still running the tape on our expenses."

NEWS NOTES

New ISMA Members

Bharat L. Agrawal, M.D., Richmond, oncology.

Hans C. Andreasen, M.D., Terre Haute, family practice.

Steve T. Arthur, M.D., Evansville, anesthesiology.

H. M. Bacchus Jr., M.D., Fort Wayne, family practice.

Ronald L. Baker, M.D., Shelbyville, obstetrics and gynecology.

Mary B. Barass, M.D., Kempton, general practice.

Steven G. Becker, M.D., Evansville, diagnostic radiology.

Antonio M. Betancourt, M.D., Bloomington, psychiatry.

Madhav H. Bhat, M.D., Fort Wayne, neurology.

Bennie C. Blake, M.D., Valparaiso, general surgery.

James F. Blechl, M.D., South Bend, family practice.

James L. Blumling, M.D., Lafayette, family practice.

Leonard Bok, M.D., Fort Wayne, radiology.

William J. Bowen, M.D., Anderson, general surgery.

David C. Brown, D.O., Markle, family practice.

Sanford A. Carson, M.D., Valparaiso, pulmonary diseases.

William M. Cockrum, M.D., Brackettville, Tex., ophthalmology.

Weldon J. Cooke, M.D., Michigan City, general practice.

John P. Cox, M.D., New Castle, diagnostic radiology.

Alan P. Culbreth, M.D., Madison, family practice.

Gerard M. Davidson, M.D, Dyer, family practice.

Mark W. DeRoo, M.D., Lafayette, pediatrics.

David A. DeSchepper, M.D., Munster, family practice.

Arthur W. DeTore, M.D., Fort Wayne, internal medicine.

Wayne H. Denton, M.D., Lafayette, psychiatry.

Rajendra S. Desai, M.D., Terre Haute, cardiovascular diseases.

Marco J. DiBiase, M.D., Michigan City, radiology.

F. H. Paul DiMaio, M.D., Logansport, otorhinolaryngology.

Robert M. Dove III, M.D., Muncie, anesthesiology.

Ahmad Dowlut, M.D., Cannelton, pediatrics.

Ray E. Drasga, M.D., Merrillville, internal medicine.

Eugene P. Durbin, M.D., Batesville, general practice.

Lewis A. David Edgeworth, M.D., Bristol, family practice.

Lorenzo A. Eli, M.D., New Castle, general practice.

Belarmino T. Frogozo, M.D., Terre Haute, plastic surgery.

Marcelo R. Gavilanez, M.D., Markle, obstetrics and gynecology.

Louis T. Greenberg, M.D., Carmel, radiology.

Carl D. Griffin, M.D., W. Lafayette, emergency medicine.

Elmo A. Griggs, M.D., Indianapolis, clinical pathology.

Vijay K. Gupta, M.D., Dyer, anesthesiology.

Gregory N. Haase, D.O., Warsaw, internal medicine.

Gary A. Hambel, M.D., Fort Wayne, cardiovascular diseases.

Steven A. Harris, M.D., Indianapolis, internal medicine.

Imad E. Horani, M.D., Fort Wayne, internal medicine.

Thomas I. Jones, M.D., Indianapolis, hematology.

U. R. Kalapatapu, M.D., Logansport, psychiatry.

James P. Kelly, M.D., South Bend, cardiovascular surgery.

Chung-Ja Kim, M.D., Valparaiso, diagnostic radiology.

Robert J. Kinsey Jr., M.D., Kokomo, obstetrics and gynecology.

Stephen A. Kissel, M.D., Greencastle, family practice.

Arthur N. Larson, M.D., Elkhart, general practice.

O. H. Lee-Johnson, M.D., Merrillville, general surgery.

Mark R. Lindenmeyer, M.D., Batesville, anesthesiology.

Alan Lloyd, M.D., Muncie, anesthesiology.

Shirley A. Madison, M.D., Indianapolis, plastic surgery.

Alberto R. Maldonado, M.D., Jeffersonville, plastic surgery.

Scott A. McPherson, M.D., Warsaw, family practice.

Shobhana D. Mehta, M.D., Terre Haute, psychiatry.

Jeffrey M. Moseman, M.D., Bloomington, family practice.

Theodore R. Neumann, M.D., South Bend, family practice.

Curtis A. Ngau, M.D., Michigan City, plastic surgery.

Gregory S. Nowak, M.D., Elkhart, anesthesiology.

Ajit V. Pai, M.D., South Bend, anesthesiology.

Matthew D. Perry, M.D., Crown Point, pathology.

Keith A. Phillips, M.D., Evansville, diagnostic radiology.

Lance A. Pickrell, M.D., Terre Haute, ophthalmology.

Richard B. Ressman, M.D., LaPorte, orthopedic surgery.

William N. Richardson, M.D., Anderson, occupational medicine.

Richard N. Rubinstein, M.D., Valparaiso, psychiatry.

M. Lynn Ryan, M.D., Lawrenceburg, pediatrics.

Jeffrey E. Salon, M.D., Fort Wayne, internal medicine.

Cynthia J. Sanders, M.D., Chicago, internal medicine.

Paul R. Sargent, D.O., Dillsboro, general practice.

Richard F. Schilling, M.D., Bloomington, family practice.

Philip A. Schneider, M.D., South Bend, therapeutic radiology.

K. Michael Schulz, M.D., Bedford, pediatrics.

David F. Sciortino, M.D., Fort Wayne, hematology.

John N. Semertzides, M.D., Lawrenceburg, general surgery.

M. Nabil Shabeeb, M.D., East Chicago, general surgery.

Ronald L. Shelton, M.D., Indianapolis, endocrinology.

Janine S. Sheppard, M.D., Indianapolis, physical medicine and rehabilitation.

Roger G. Spahr, M.D., Indianapolis, family practice.

Matthew J. Sprunger, M.D., Fort Wayne, obstetrics and gynecology.

Harry L. Staley, M.D., Indianapolis, rheumatology.

D. Mark Stinson, M.D., Anderson, family practice.

Larry L. Strong, M.D., Gary, urological surgery.

Charles R. Taylor, M.D., Greenfield, cardiovascular diseases.

Frank A. Utes, D.O., Winamac, general practice.

Jerrold A. VanDyke, M.D., South Bend, diagnostic radiology.

Daniel J. Wickert, M.D., Lafayette, obstetrics and gynecology.

Alan C. Williams, M.D., Michigan City, diagnostic radiology.

Robert L. Winders, M.D., Greencastle, general surgery.

Dennis D. Woodhall, M.D., Muncie, cardiovascular surgery.

Residents:

William K. Adair, M.D., Muncie, internal medicine.

Jacqueline L. Akey, M.D., Fort Wayne, family practice.

Sandra L. Aspy, M.D., Fort Wayne, family practice.

William J. Berghoff, M.D., Fort Wayne, family practice.

Jeffrey W. Bragg, D.O., Muncie, family practice.

Peter G. D'Amour, M.D., Indianapolis, diagnostic radiology.

Anita K. Das, M.D., Indianapolis, family practice.

Curtis K. Deason, M.D., Fort Wayne, family practice.

Gerry S. Easterday, M.D., Fort Wayne, family practice.

Weldon T. Egan, M.D., Indianapolis, anesthesiology.

Rex A. Flenar, M.D., Fort Wayne, family practice.

Sudhakar R. Garlapati, M.D., Merrillville, family practice.

Jon T. Harman, M.D., Indianapolis, radiology.

Stephen J. Jasinski, M.D., Fort Wayne, family practice.

Constance S. Kayser, M.D., Indianapolis, neurological surgery.

John M. Kosta, M.D., Plainfield, otorhinolaryngology.

John F. Maesaka, M.D., Fort Wayne, family practice.

John E. Marvel, M.D., Indianapolis, therapeutic radiology.

Christopher M. Nixon, M.D., Fort Wayne, family practice.

Mary A. O'Brien, M.D., Fort Wayne, family practice.

Charles L. F. Richert, M.D., Greenwood, family practice.

Jerome E. Stasek Jr., M.D., Indianapolis, internal medicine.

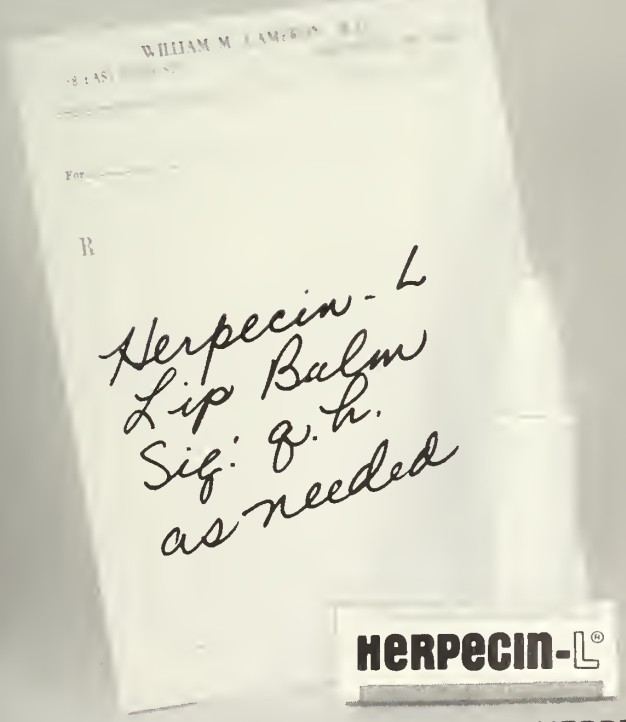
Brenda S. Stiles, M.D., Fort Wayne, family practice.

Randall R. Stoltz, M.D., Evansville, family practice.

Paul D. West, M.D., Indianapolis, anesthesiology.

Dawn M. Zimmer, M.D., Indianapolis, obstetrics and gynecology.

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NEWS NOTES

Here and There . . .

Dr. John C. Johnson, director of Emergency Medical Services at Porter Memorial Hospital, Valpraiso, has been elected to the board of directors, American College of Emergency Physicians.

Dr. Michael K. Crider of Muncie has been certified by the American Board of Dermatology.

Dr. Gordon Hughes, an internal medicine resident at Ball Memorial Hospital, Muncie, has been elected as at-large member of the American Society of Internal Medicine's governing council for its new Resident Physicians Section.

Dr. Randolph Lievertz of Indianapolis recently spoke on pelvic inflammatory disease with the medical staff of Clark County General Hospital and on chronic obstructive pulmonary disease with the medical staff of Union Hospital, Terre Haute; he also has been a guest on WISH-TV's "Indy Today" show.

Dr. Parker W. Snyder of Peru has been re-elected Miami County health officer.

Dr. William C. Heilman Jr., a New Castle family physician, has retired after practicing 31 years; he was president of the New Castle Clinic.

Dr. Rodney A. Mannion of LaPorte discussed "Female Urinary Incontinence" at LaPorte Hospital in January.



"Some days I don't feel I'm serving all of humanity—just the insurance companies."

Dr. William D. Carter, associated with the South Bend Memorial Family Practice Residency Program, has been awarded a postgraduate fellowship by the College of Human Medicine of Michigan State University.



Dr. Bryan

Dr. Franklin A. Bryan of Fort Wayne has retired from administrative and faculty appointments with the I.U. School of Medicine; he had been associate dean of the Fort Wayne center since 1970.

Dr. Mark T. Adams of Fort Wayne has been elected to fellowship in the American Academy of Pediatrics.

Dr. Donald C. McCallum of Franklin has been re-elected chief of the medical staff at Johnson County Memorial Hospital; Dr. Peggy L. Kovach is secretary.

Dr. James E. Reidy is the new president of the medical staff at St. Joseph's Medical Center, South Bend; Dr. Douglas J. Wilson is vice-president, and Dr. John Reed is secretary-treasurer.

Dr. James D. Rogge is the new president of the medical staff at St. Francis Hospital, Beech Grove; Dr. Donald J. Kerner is vice-president and president-elect, and Dr. Stafford W. Pile is secretary-treasurer.

Dr. James J. Harris is the new president of the medical staff at Parkview Memorial Hospital, Fort Wayne; Dr. William B. Rank is president-elect, and Dr. James E. Albright is secretary-treasurer.

Dr. Daniel B. Roberts of Peru is the new president of the medical staff at Dukes Memorial Hospital; Dr. Maurice D. Sixbey is vice-president, and Dr. Rhys D. Jones is secretary.

Dr. Peter R. Skafish is the new president of the medical staff at LaPorte Hospital; Dr. Barbara Backer is vice-president, and Dr. Robert M. Kelsey is secretary-treasurer.

Dr. Edward Ross of Indianapolis is the new president of the Indiana Society of Internal Medicine; Dr. L. Craig Miller of Danville is president-elect, and Dr. Robert L. Rudesill of Indianapolis is secretary-treasurer. New members of the ISIM Council are Drs. Paul Batties, Ramon Dunkin, David K. Johnloz, Debra J. Myers, Cheryle D. Southern, Andrew C. Thieneman Jr., and Ralph B. Ullom.

Dr. Virgil C. McMahan, a Vincennes orthopedic surgeon, has retired from practice, ending a medical career that began in 1940.

Dr. Robert S. Kepner, an Anderson pediatrician, spoke in January with the local chapter of the "Just Say No Club," which consists of fourth, fifth and sixth graders in the Anderson community school system; he spoke on the dangers of drug involvement.

Dr. Stephen W. Perkins of Indianapolis has attained full fellowship with the American College of Surgeons.

Dr. Anthony H. Horan, a South Bend urologist, lectured at the 1986 Testis Workshop at Vanderbilt University; his subject was "The Etiology of Testicular Atrophy in the Cryptorchid Testis of Man: A Thought Experiment and Information Synthesis."

Dr. Alan R. Gilbert, a Fort Wayne dermatologist, discussed a variety of skin care issues during a public health program conducted in Roanoke in January.

Dr. George W. Hicks of Indianapolis presented a paper at the recent annual meeting of the Middle Section of the American Laryngological, Rhinological and Otological Society in Cleveland; it was entitled, "A Review of 925 Cases of Tympanoplasty Using Formaldehyde-Formed-Fascia Grafts."

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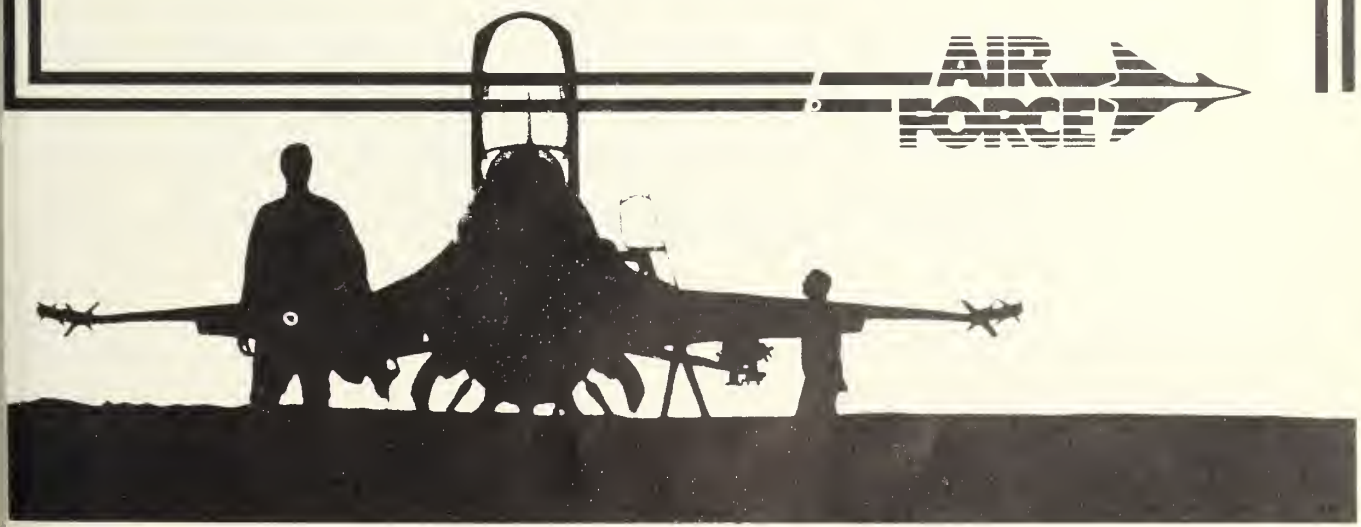
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10 – Frank M. Sturdevant, Valparaiso (1988)
11 – Michael S. Liebner, Logansport (1989)
12 – Thomas A. Felger, Fort Wayne (1989)
13 – Alfred C. Cox, South Bend (1988)
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Peter R. Petrich, Attica (1987)
Thomas C. Tyrrell, Hammond (1987)
Everett E. Bickers, Floyds Knobs (1988)
Alvin J. Haley, Carmel (1988)
John A. Knote, Lafayette (1988)

AMA ALT. DELEGATES (Terms end Dec. 31)
Martin J. O'Neill, Valparaiso (1987)
Herbert C. Khalouf, Marion (1987)
Vincent J. Santare, Munster (1987)
Edward L. Langston, Flora (1988)
George T. Lukemeyer, Indianapolis (1988)
Robert M. Seibel, Nashville (1988)

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1 – Pres: Gary L. Beck, Evansville
Secy: Alan H. Johnson, Evansville
Annual Meeting: May 21, 1987, Evansville
2 – Pres: Ernest DuPre, Sullivan
Secy: Betty J. Dukes, Dugger
Annual Meeting: May 14, 1987, Sullivan
3 – Pres: Marvin L. McClain, Scottsburg
Secy:
Annual Meeting: May 7, 1987, Scottsburg
4 – Pres: Manuel G. Garcia, Batesville
Secy:
Annual Meeting: May 6, 1987, Batesville
5 – Pres: William L. Strecker, Terre Haute
Secy: Peggy Sankey-Swaim, Rockville
Annual Meeting: Sept. 9, 1987, Terre Haute
6 – Pres: Douglas Morrell, Rushville
Secy: Robert J. Warren, Richmond
Annual Meeting: May 13, 1987, Richmond
7 – Pres: Peter L. Winters, Indianapolis
Secy: H. Marshall Trusler, Indianapolis
Annual Meeting: April 1987, Indianapolis
8 – Pres: Lily A. Ly, Portland
Secy: Kathleen A. Galbraith, Portland
Annual Meeting: June 3, 1987, Portland
9 – Pres: Norbert M. Welch, Lafayette
Secy: Max N. Hoffman, Covington
Annual Meeting: June 10, 1987, Lafayette
10 – Pres: Vincent J. Santare, Munster
Secy: Barron M. Palmer, Hammond
Annual Meeting: Sept. 23, 1987
11 – Pres:
Secy:
Annual Meeting: Sept. 16, 1987, Logansport
12 – Pres: Anthony Donesa, Fort Wayne
Secy: Mark S. Souder, Auburn
Annual Meeting: Sept. 17, 1987
13 – Pres: Donald W. Smith, South Bend
Secy: Thomas J. Eberts, South Bend
Annual Meeting: Sept. 9, 1987, South Bend

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Karyl Kirkbride, Convention Coordinator
Tom Martens, Members' Health Insurance
Carol Ann Cunningham, Resident Medical Society, Specialty Society Services
Martin Badger, INDIANA MEDICINE

OBITUARIES

Harlan H. Tyner, M.D.

Dr. Tyner, 71, a retired Indianapolis ophthalmologist, died Nov. 30 at his home.

He was a 1942 graduate of Indiana University School of Medicine and was a veteran of World War II.

Dr. Tyner, who retired in 1985, was a diplomate of the American Board of Ophthalmology and was a fellow of the American Academy of Ophthalmology.

John B. Anderson, M.D.

Dr. Anderson, 63, a Vincennes surgeon 33 years, died Dec. 8 at Good Samaritan Hospital.

He was a 1951 graduate of Washington University School of Medicine, St. Louis, and was an Army veteran of World War II.

Dr. Anderson was a former president of the Knox County Medical Society. He was a member of the American Society of Abdominal Surgeons and the American Geriatrics Society.

Jerome A. Graf, M.D.

Dr. Graf, 82, a retired Bloomfield anesthesiologist, died March 10, 1986.

He was a 1940 graduate of Indiana University School of Medicine and an Army veteran of World War II.

Dr. Graf was a senior member of the Greene County Medical Society and a former ISMA delegate.



Dr. Beeler

Charles M. Gruber Jr., M.D.

Dr. Gruber, 71, a retired Indianapolis physician, died Dec. 22 at St. Vincent Hospital.

He was a 1941 graduate of Jefferson Medical College, Philadelphia, and a World War II Army veteran.

Dr. Gruber, who retired in 1985, had been engaged in clinical research for Eli Lilly and Company 31 years. He was Board-certified in internal medicine and was a member of the American College of Physicians and the American Society for Clinical Pharmacology and Therapeutics.

John W. Beeler, M.D.

Dr. Beeler, 65, an Indianapolis radiologist who served as ISMA president from 1976 to 1977, died Jan. 15 at Indiana University Hospital.

He was a 1944 graduate of Indiana University School of Medicine. He served in the Army Air Corps from 1945 to 1947 and with the Army Medical Department from 1953 to 1954.

Dr. Beeler was a private practitioner and an associate professor of radiology at I.U. School of Medicine. He served on the board of directors of Blue Shield of Indiana from 1958 to 1986, and he was formerly a member of the board of directors, National Board of Medical Examiners.

Dr. Beeler's professional affiliations included the American College of Radiology and the American Roentgen Ray Society. He also was a member of the Radiological Society of North America, of which he was a past president.

Forrest E. Kirshman, M.D.

Dr. Kirshman, 85, a retired Muncie physician, died Dec. 25 at Ball Memorial Hospital.

He was a 1927 graduate of Indiana University School of Medicine and an Army veteran of World War II.

Dr. Kirshman retired from private practice in 1971, but then served eight years as staff physician at Ball State University's Amelia T. Wood Health Center. He was a member of the Delaware-Blackford County Medical Society, the Muncie Academy of Medicine, and the ISMA Fifty Year Club.

Kenneth W. Caldwell, M.D.

Dr. Caldwell, 59, a Connersville radiologist, died June 25, 1986.

He was a 1948 graduate of Temple University School of Medicine, Philadelphia.

Dr. Caldwell was Board-certified and was a fellow of the American College of Radiology and the American Academy of Family Physicians.

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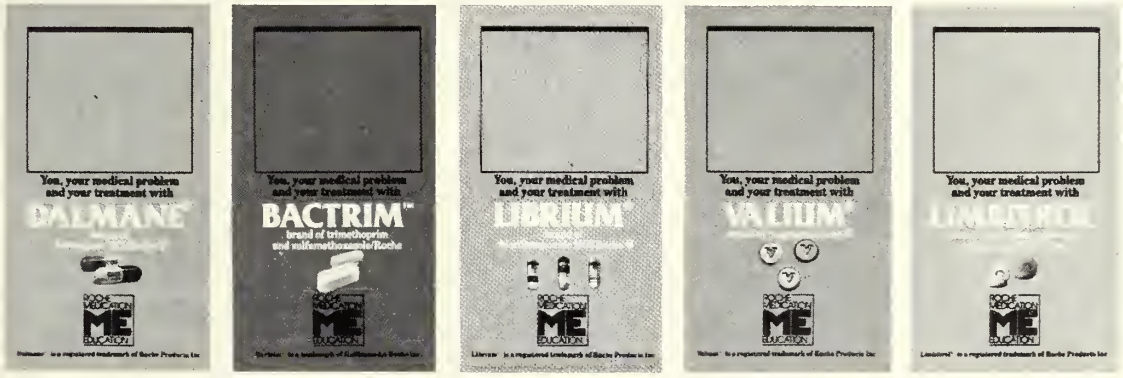
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APRIL 1987

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MEDICAL MUSEUM NOTES

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CHARLES A. BONSETT, M.D., Indianapolis

THESE TWO ITEMS from 1853 issues of the Indianapolis *Locomotive* tell something about the practice of medicine in Indiana at that time.

(March 5, p. 4): When men are sick they want to be cured, cost what it may, but when they are on their feet, and at their business again, they do not want to pay, especially if the bill is a little one. The poor doctor is called from his bed on a stormy night with the stirring summons, "Doctor—want you to come right straight away off to Banks'. His child's dead."

"Then why do you come?"

"He's p'isoned. They gave him laud'num for paregoriky."

The doctor pushes off through the storm, meets with diverse mishaps by the way, and at length arrives at the house of his poisoned patient. He finds all closed—not a light to be seen.

"I knocked at the door but no answer. I knocked furiously, and at last a night-cap appeared from the window, and a woman's voice squeaked out—"Who's there?"

"The doctor, to be sure; you sent for him. What the dogs is the matter?"

"Oh, it's no matter, doctor. Ephraim is better. We got a little skerred kind'o. Gin him laud'num, and he slept kind'o sound, but he's woke up now."

"How much laudanum did he swallow?"

"Only two drops. 'Taint hurt him none . . . wonderful bad storm tonight."

The doctor turns away, buttoning up his overcoat under his throat, to seek his home again, and tries to whistle away his mortification and anger, when the voice calls.

"Doctor, Doctor!"

"What do you want?"

"You won't charge nothin' for this visit, will you?"

(August 13, p. 2): I was sent for in great haste to attend a gentleman of respectability who had been discovered in his room lying senseless on the floor. On arriving at the house, I found Mrs. H. in great distress of mind. "What is the matter with Mr. H?" I asked. . .

"I'm afraid it is apoplexy," she replied. "I found him lying upon the floor where he had, to all appearances, fallen suddenly from his chair. His face is purple, and though he breathes, it is with great difficulty."

I went up to see my patient. He had been lifted from the floor and was now lying upon the bed; sure enough, his face was purple and breathing labored, but somehow the symptoms did not indicate apoplexy. . . .

"Hadn't he better be bled, doctor?" asked the anxious wife.

"I don't know that it's necessary," I replied. "I think if we let him alone it will pass off in the course of a few hours."

". . . Won't you bleed him, doctor? A few ounces of blood taken from his arm may give life to the now stagnant circulation of the blood . . ."

Thus urged, I, after some reflection, ordered a bowl and bandage and, opening a vein, relieved him of about eight ounces of blood. But he lay as insensible as before, much to the distress of his poor wife.

By this time, several relatives and friends, who had been sent for, arrived and urged upon me the adaptation of some active means of restoring the sick man to consciousness . . .

. . . I suggested a stomach pump, (but) the wife was offended. I was not the regular family physician. (I) had been called in to meet the alarming emergency because my office happened to be nearest. Feeling my position to be a difficult one, I suggested that the family physician had better be called.

When Dr. S. arrived, I gave him my views of the case and stated what I had done and why I had done it. We then proceeded to the bedside of our patient; there were still no signs of approaching consciousness. "Don't you think his head must be shaved and blistered?" asked the wife anxiously. Dr. S. thought a moment and then said, "Yes, by all means, send for a barber, and also a fresh fly blister, four inches by nine."

I looked into the face of Dr. S. with surprise; it was perfectly grave and earnest. I hinted my doubt of the good that mode of treatment would do; but he spoke confidently of the result and said that it not only would cure the disease but, he believed, take away the predisposition thereto, to which Mr. H. was affected to a high degree.

The barber came. The head of Mr. H. was shaved and Dr. S. applied the blister with his own hands, which completely covered the scalp from forehead to occiput.

The blister began to draw. No signs of returning consciousness showed themselves further than an occasional low moan or an uneasy tossing of the arms. For two full hours the burning plaster parched the tender skin of his shorn head and was then removed; it had done good service.

Just then the eyes of Mr. H. opened, and he looked with half stupid surprise from face to face, of the anxious group that surrounded the bed. "What in the mischief is the matter?" he at length said. At the same time, feeling a strange sensation about his head, he placed his hand rather heavily thereon. "Heavens and earth!" He was now fully to his senses. "Heavens and earth. What ails my head? Where is my hair?"

The facts of the case were these: H. had a weakness; he could not taste wine or strong drink without being tempted to excess . . . He had shut himself up at home for a time to see if total abstinence would give him strength. He got along well for a few days, particularly so, as his coachman kept a well filled bottle for him in the carriage house to which he not infrequently resorted; but a too frequent devotion to this bottle brought on the supposed apoplexy.

Dr. S. was right in his mode of treating the disease after all, and did not err in supposing it would reach the predisposition. The cure was effectual. . . .

WHAT'S NEW?

News of what is new in the medical supply industry is composed of abstracts from news releases by book publishers and manufacturers of pharmaceuticals, clinical laboratory supplies, instruments and surgical appliances. Each item is published as news and does not necessarily constitute an endorsement of a product or recommendation for its use by INDIANA MEDICINE or by the Indiana State Medical Association.

Med-Systems Management of Dayton has several systems designed to improve the efficiency of doctors' private offices. Physician Fee Management reviews and analyzes fee structure, and advises on office procedures which should be included in fee structure. Total Facilities Management Program turns offices into profitable and efficient practices without raising fees. The newest service is Guaranteed Income. The overall programs cover marketing, advertising, merchandising, sales promotion and public relations.

Stryker Medical Division is introducing a Stretcher/Chair system for same-day surgery. Model 966 Head-Neck Surgery Bed is a wheeled stretcher that functions for Pre-Op, Surgery and Recovery. Its special features include Trendelenburg Position, 5th Wheel Steering, Foot Control Hydraulics, sturdy siderails and some exclusive options such as the Stryker AirFlo™ system that circulates fresh oxygen to the patient's draped face.

Aircast, Inc. has an Ankle Brace especially suited to pediatric patients and to adults shorter than 5'2". Preinflated aircells and strategically placed cups to accommodate the malleoli make the device highly supportive without undue pressure.

Abbott Laboratories has introduced a new tablet for its Tranxene antianxiety drug. The tablet replaces Tranxene capsules and will make it easier for patients to distinguish the product from other medications. Called "T-TAB", it has a distinct six-sided shape with a debossed "T" on one side. Distinctive tablet shapes and colors help assure patient compliance, especially for the elderly patient.

Abbott Laboratories is marketing the first test for detection of the deadliest form of hepatitis, delta hepatitis. The laboratory has also received FDA approval for marketing a genetically engineered hepatitis B test. Abbott now markets nine different hepatitis tests.

Gower Publishing has released a revised edition of *Philosophy and Medicine*. The author, Dr. E. K. Lederman, published the first edition in 1970. The new work enlarges the discussion by including the metaphysical and epistemelogical aspects of medicine. 180 pages, $41.50.

Year Book Medical Publishers have released *Head and Neck Cancer: Clinical Decisions and Management Principles*. It is a reference book of 538 pages and 258 illustrations, edited by a group headed by Dr. Donald G. McQuarrie of the University of Minnesota. It has received compliments from *The New England Journal of Medicine*—"A unified, complete, and well-edited book comfortable to read and handle, the material is well selected." $125.

International Bio-Medical Information Service announces the 4th edition of *The Medical and Healthcare Marketplace Guide*. It has several new features in addition to the standard elements that have made this book so widely quoted. It lists and describes 4,482 firms in the health care industry and it has listings for 1,500 medical and health care services firms. $290.

Compact Books will soon release a new book, *Ear Infection in Your Child*, written by Kenneth Grundfast, M.D. and Cynthia Carney. It is for parents but may also be instructive for pediatricians, family practitioners, otolaryngologists, educators, speech language therapists and audiologists. $14.95.

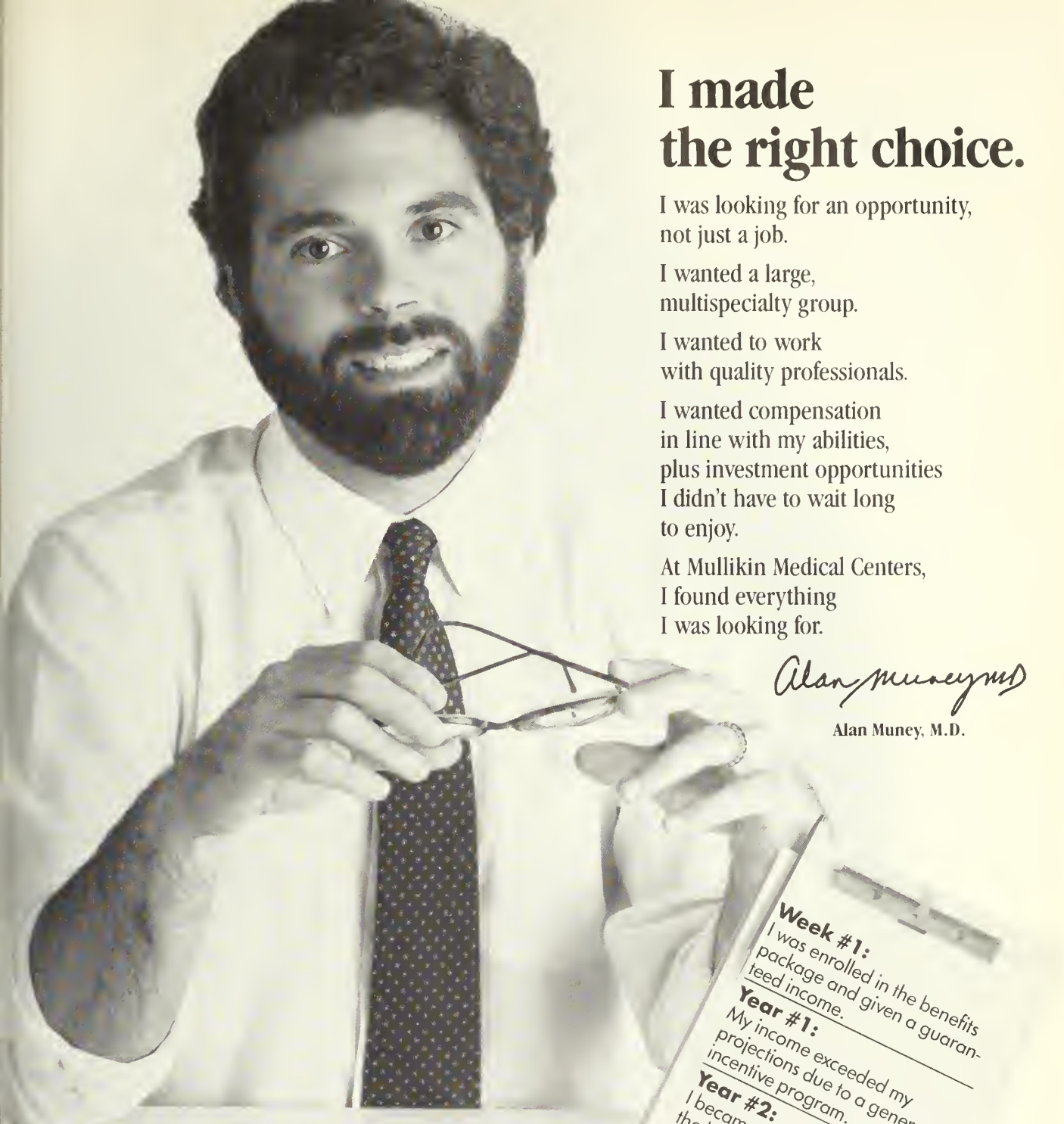
Gower Publishing announces *The Health Information Handbook*. The author is Robert Gann. The book was written because of the unprecedented explosion of interest in the participation of people in their own health care. It covers responsibility for health, the informed patient, health information in the UK, health information in other countries, and collecting and organizing health information. 251 pages. $41.95.



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FUTURE FILE

Practice Management

The ISMA and the Resident Medical Society will co-sponsor a practice management workshop April 24 and 25 at St. Vincent Hospital, Indianapolis.

Staff from the AMA Dept. of Practice Management will discuss patient relations, accounting systems, personnel management, third-party payers and medical records. ISMA legal counsel will review corporate and malpractice law requirements in Indiana.

Registration fees have been discounted for ISMA members, their spouses and office staff. For more information, contact Carol Ann Cunningham at ISMA headquarters, Indianapolis.

Microsurgical Solutions

"Microsurgical Solutions to Reconstructive Problems in the Upper Extremity" is the title of a course scheduled for May 9 in Chicago.

The course is being sponsored by the American Society for Surgery of the Hand. Dr. James B. Steichen of Indianapolis will be one of the faculty members.

For more information, contact ASSH at 3025 S. Parker Road, Suite 65, Aurora, Colo. 80014.



"We can't find a replacement while you're on vacation, Smogg, but we've decided it doesn't matter."

The *Journal of the American Medical Association* publishes a list of CME courses for the United States twice yearly. The January listing features courses offered from March through August; the July listing features courses offered from September through February.

St. Vincent Hospital CME

St. Vincent Hospital and Health Care Center, Indianapolis, announces the following CME programs:

April 8-10: Midas Rex Hands-on Orthopedic Workshop, Sheraton Marten House, Indianapolis.

April 25: Fifth Annual Spring Seminar in Dermatopathology; Hideko Kamino, M.D., guest lecturer; St. Vincent Hospital.

May 1-2: Seventh Annual Joseph C. Finneran Professorship, Witold J. Rudowski, M.D., Director, Dept. of Surgery, Research Institute of Hematology and Blood Transfusion, Warsaw, Poland; Cooling Auditorium, St. Vincent Hospital.

May 22: Annual "500" Orthopedic Conference, Cooling Auditorium, St. Vincent Hospital.

For more information, contact Marilyn Soltermann, CME coordinator—(317) 871-3460.

Computers in Primary Care

An Anglo-American conference on "The Future of Computers in Primary Care" will be held May 13-15 at the University of Cincinnati Medical Center.

The conference will focus on the future integration of computer technology with the practice of primary care in the U.S., Great Britain and Canada. It is sponsored by the Royal Society of Medicine, the Society of Teachers of Family Medicine, and the Dept. of Family Medicine, University of Cincinnati.

For details, contact John R. Kues, Ph.D., Dept. of Family Medicine, 231 Bethesda Ave., Cincinnati, Ohio 45267—(513) 872-4066.

Hand Surgery

"Management of Congenital Deformities of the Upper Extremity: Contemporary Views on the Treatment of the Radial Club Hand" is the title of the monthly Monday Night Hand Surgery Conference to be held April 20 at the Indiana Center for Surgery and Rehabilitation of the Hand, Indianapolis. Dr. William B. Kleinman will be the speaker.

The conference begins at 7 p.m. These Monday Night Hand Surgery Conferences are presented each month as continuing education for hand fellows, orthopedic residents, hand therapists and others interested in surgery of the upper extremity.

For information on this and future conferences, call Beth Bush at (317) 875-9105.

Indiana University CME

May 6-7: 22nd Annual Indiana Multidisciplinary Child Care Conference, Holiday Inn-Union Station, Indianapolis.

May 6-8: Radiology Update, Hyatt Regency, Indianapolis.

May 9: Current Trends in Orthopedic Hip Surgery, Radisson Hotel, Indianapolis.

May 10: OB-GYN Update, Sheraton Marten House, Indianapolis.

May 12-14: Family Practice Update Part I, Holiday Inn-Airport, Indianapolis.

May 14-15: 1987 Symposium on Ultrasound on the Breast, Holiday Inn-Airport, Indianapolis.

May 20: Alumni Day CME Program for Internists, I.U. Medical Center, Indianapolis.

June 17-18: Pediatric Critical Care in Perspective, Sheraton Meridian, Indianapolis.

July 6-15: The Applied Anatomy and Histopathology of the Head and Neck and Temporal Bone, I.U. Medical Center, Indianapolis.

For further information on these and other CME programs, contact Melody Dian, Assistant Director, CME, I.U. School of Medicine—(317) 274-8353.

Methodist Hospital CME

May 1: 13th Annual William Niles Wishard Jr. Memorial Lecture, Methodist Hospital, Indianapolis.

May 14-15: 22nd Annual Gordon W. and Mae Batman Lecture Series, Methodist Hospital, Indianapolis.

June 6: High Energy Fractures: External Fixation and Locking Nails, Methodist Hospital auditorium, Indianapolis.

June 24-26: 8th Annual Scientific Meeting of the American Society for the Immunology of Reproduction, Hilton-on-the-Circle, Indianapolis.

(April courses are listed in the February 1987 issue of INDIANA MEDICINE, page 130.)

For more information, contact Dixie Estridge, CME coordinator, Graduate Medical Center, Methodist Hospital of Indiana—(317) 929-3733.

Nutrition Update

"Nutrition Update-1987" will be the theme of the Indiana Society of Parenteral and Enteral Nutrition's annual meeting, scheduled for 9 a.m. to 4 p.m., Wednesday, April 29, at the Holiday Inn North, Indianapolis.

Several prominent national speakers will be featured. The registration fee is $25. For more information, call Dr. Joseph Misinski at (317) 871-2122.

SIDS Workshop

Sudden Infant Death Syndrome (SIDS) and infantile apnea will be the subject of an Indiana State Board of Health workshop scheduled for Friday, April 24. It will be conducted from 8:30 a.m. to 3:45 p.m. at the Holiday Inn Holidome in Columbus, located at I-65 and SR 46.

The keynote address will be presented by Dr. George Little, chairman of the National Institutes of Health Consensus Development Panel on Infantile Apnea and Home Monitoring.

Registration after April 10 is $25. For more information, call (317) 633-8459.

Diet for the Elderly

"Drug and Diet Prescribing for Major Medical Problems of the Elderly" will be discussed Thursday, April 16, at the Marriott Inn, Indianapolis.

For more information on this CME program, contact Carolyn Roeder, Medical Education, Community Hospitals Indianapolis—(317) 353-4269.

Roentgen Society to Meet

"RAPs and Other Dirty Words" will be the topic of Otha W. Linton, associate executive director of the American College of Radiology, featured guest speaker at the Indiana Roentgen Society meeting Sunday, May 3, at the Holiday Inn North, Indianapolis.

Mr. Linton's presentation—RAPs is an acronym for radiologists, anesthesiologists and pathologists—will follow the annual general membership meeting, which begins at 10 a.m.

To register for the meeting, call Carol Ann Cunningham at (317) 925-7545 or 1-800-382-1721, toll-free in Indiana.

Hypnotherapy Workshop

The Menninger Foundation will conduct an Introductory Workshop in Hypnotherapy May 7-9 in Topeka, Kansas.

To register and for additional information, contact Brenda Vink, Menninger Foundation, Box 829, Topeka, Kansas 66601—(913) 273-7500, ext. 5992.

Interoperative Radiation

"Interoperative Radiation: A New Combined Treatment Approach to Cancer" is the title of a CME course to be conducted July 18 at the University of Kansas Medical Center, Kansas City. Credit is granted by the AMA, the AAFP and CNE.

The correspondent is Eileen Buttron, Office of CME, 39th and Rainbow Blvd., Kansas City, Kansas 66103—(913) 588-4480.

Child Care Conference

The 22nd Annual Indiana Multidisciplinary Child Care Conference will be held May 6 and 7 at the Union Station Holiday Inn in downtown Indianapolis.

The speakers and subjects will include: Dr. Ellen Wald—Pediatric Infectious Diseases; Dr. Jan Paradise—Pediatric Gynecology in Children and Adolescents; Drs. N. Jeffrey Maisels and Richard Schreiner—Neonatalogy; Dr. Robert Blum—Adolescent Drug and Substance Abuse; Dr. David Rothner—Pediatric Neurology; and Dr. William Weston—Pediatric Dermatology.

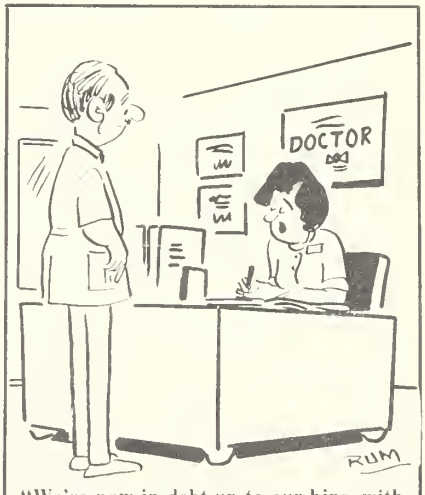
Contact Dr. Morris Green, I.U. School of Medicine, Riley Hospital for Children, 702 Barnhill Drive, Indianapolis 46223.

Schizophrenia

"The Genesis of Schizophrenia" is the title of a symposium to be conducted June 22-24 at the Menninger Foundation. The fee is $185.

For a program and details, contact Donna J. Smith, Menninger Foundation, Box 829, Topeka, Kansas 66601—(913) 273-7500, ext. 5992.

CONTINUED ON PAGE 368



"We're now in debt up to our hips, with a very good chance of being up to our ears in four months and over our heads in five."

CANCER CORNER

WILLIAM M. DUGAN, JR., M.D.
Methodist Hospital Cancer Care Center, Indianapolis

I CAN COPE series continues. The I Can Cope Cancer Education series enables the patients and their families an opportunity to acquire information about their disease, diagnostic procedures, treatment, and self-care management. The importance of attitude is explored as those involved learn effective ways of coping with cancer's impact on physical and emotional well being. The program also acquaints patients with the many resources available in the community. Classes are mainly informational, although there is opportunity to share experiences with other participants.

The classes are taught by a cross-section of volunteer health care professionals and many veterans of past I Can Cope programs. The program includes coping with facts about cancer, coordinating diet and activity, normal living adjustments, evaluating your feelings, and resources for living.

For further information regarding this program in your area or starting an I Can Cope series contact your local ACS chapter.

THE EXPANDING ROLE OF REHABILITATION IN CANCER CARE is an audiotape of the 1986 John E. Stanwood Lectureships provided by the Good Samaritan Hospital and Medical Center, Comprehensive Cancer Program in Portland, Oregon.

The conference is conducted semi-annually by the Cancer Rehabilitation Service at Good Samaritan Hospital. For a complete listing of tapes available or information regarding the conference write: Good Samaritan Hospital & Medical Center, Comprehensive Cancer Program, Cancer Rehabilitation, 1015 N.W. 22nd Ave., Portland, Oregon 97210.

THE REALITIES OF CANCER IN MINORITY COMMUNITIES is the title of M.D. Anderson Hospital and Tumor Institute's symposium that is to be held April 22-25.

The goal of the symposium is to stimulate discussion of recent advances in basic and clinical research and their application in the prevention and treatment of cancer in minority and economically disadvantaged groups. The symposium is a continuing medical education activity for 18 credit hours in the Category 1 of the Physicians' Recognition Award of the American Medical Association.

INTRODUCTION TO PSYCHO-SOCIAL ONCOLOGY is the program sponsored by Sloan-Kettering Cancer Center at New York City, April 22-24. Information can be obtained by contacting Lisa Griffin, Course Secretary, Department of Social Work, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, N.Y. 10021.

NEW STRATEGIES IN THE MANAGEMENT OF LUNG CANCER, sponsored by the R. Livingston Ireland Cancer Center at Cleveland, will be held April 25. For further information contact Barbara Guy, Ireland Cancer Center, Lowman Building-211, University Hospitals of Cleveland, 2074 Abington Road, Cleveland, Ohio 44106, or call 216/844-7856.

PEDIATRIC ONCOLOGY AND HEMATOLOGY: PERSPECTIVES ON CARE, serves as a comprehensive reference for anyone involved in treating and managing pediatric oncology and hematology patients. Edited by Marilyn J. Hockenberry, R.N., M.S.N., P.N.P. and Deborah K. Coody, R.N., M.S.N., P.N.P.: with 30 contributors, the book is divided into four detailed sections that explore childhood malignancies, hematologic disorders of children, treatment modalities, and psychosocial aspects of care. Case studies and nursing care protocols for each major disease.

Both of the above mentioned books are available through the C.V. MOSBY Company, 11830 Westline Industrial Drive, P.O. Box 28430, St. Louis, Missouri 63146.

INTERNATIONAL MEETINGS: July 19-24, XV International Congress of Chemotherapy will be held in Istanbul, Turkey. This congress is sponsored by ICC. Further information can be obtained by contacting the Secretariat, Kongresist, 193 Cumhuriyet, Caddesi D.6, Elmadey, 80203, Istanbul, Turkey.

The annual meeting of the International Society of Hematology will be held September 6-10 in Ibadan, Nigeria. Sponsored by the International Society of Hematology. Inquiries can be directed to the International Society of Hematology, Junin 1284, Buenos Aires, Argentina 1113. 54-1-83-5621.

DECISION-MAKING IN ONCOLOGIC NURSING by Susan B. Baird, R.N., M.P.H. covers cancer prevention and early detection, patient education and information, patient and family coping, comfort, nutrition, protective mechanism, mobility, bowel and urinary elimination, sexuality, ventilation, clinical emergencies and professional practice issues.

THE BASICS OF HOSPICE, a brochure recently published by the American Cancer Society, describes hospice as a concept of care for terminally ill patients, rather than as a specific place of care.

Produced in conjunction with the National Hospice Organization, the publication provides insights into the kind of care available to the dying patient and family members through hospice programs. The brochure places special emphasis on the efforts of hospice to make patients as comfortable as possible in the familiar surroundings of their homes, and to counsel family members with the pending loss. The brochure can be used as a reference source for health professionals, an informational source for patients on how and where they can receive hospice care, and an incentive for health professionals' participation in hospice care.

To show you how many hypertensives stayed on INDERAL® LA (PROPRANOLOL HCl)

after a major nationwide trial...




...we had
to find
just the
right room.

60,073 patients (90%) who started on INDERAL® LA stayed on INDERAL LA.[1*]

Surprising? Not really.

Because most patients on INDERAL LA (propranolol HCl) don't even know it's working.
A recent double-blind, placebo-controlled, crossover study in 138 hypertensive patients[2] revealed that INDERAL LA has a side effects profile unsurpassed by atenolol or metoprolol—which shows how well-tolerated once-daily INDERAL LA can be.

Sole therapy or concomitant therapy? Fifty-nine percent of the time, INDERAL LA stood on its own.

The patients in the nationwide compliance trial were no different from yours. Generally when the antihypertensive regimen is complicated, compliance may become a problem. So, the effectiveness of INDERAL LA as once-daily monotherapy is a big plus. Of the remaining hypertensives in the program, 36% were controlled merely with the addition of a diuretic to INDERAL LA.

For the noncompliant patients in your practice, INDERAL LA may well be the answer.

Almost 20,000 of the patients in the nationwide compliance trial were identified as having been noncompliant with their previous antihypertensive therapy. Their physicians reported that 88% showed improved compliance when placed on once-daily INDERAL LA.

Control, comfort, and compliance

ONCE-DAILY
INDERAL® LA
(PROPRANOLOL HCl) LONG ACTING CAPSULES

Like conventional INDERAL Tablets, INDERAL LA should not be used in the presence of congestive heart failure, sinus bradycardia, cardiogenic shock, heart block greater than first degree, and bronchial asthma.

*After a 30-day trial with INDERAL LA, physicians reported that 90% of the patients would remain on INDERAL LA.

The one you know best keeps looking better

Please see next page for brief summary of prescribing information

The one you know best keeps looking better

BRIEF SUMMARY *(FOR FULL PRESCRIBING INFORMATION, SEE PACKAGE CIRCULAR.)*

INDERAL® LA brand of propranolol hydrochloride **(Long Acting Capsules)**

DESCRIPTION. Inderal LA is formulated to provide a sustained release of propranolol hydrochloride. Inderal LA is available as 80 mg, 120 mg, and 160 mg capsules.

CLINICAL PHARMACOLOGY. INDERAL is a nonselective beta-adrenergic receptor blocking agent possessing no other autonomic nervous system activity. It specifically competes with beta-adrenergic receptor stimulating agents for available receptor sites. When access to beta-receptor sites is blocked by INDERAL, the chronotropic, inotropic, and vasodilator responses to beta adrenergic stimulation are decreased proportionately.

INDERAL LA Capsules (80, 120, and 160 mg) release propranolol HCl at a controlled and predictable rate. Peak blood levels following dosing with INDERAL LA occur at about 6 hours and the apparent plasma half-life is about 10 hours. When measured at steady state over a 24-hour period the areas under the propranolol plasma concentration-time curve (AUCs) for the capsules are approximately 60% to 65% of the AUCs for a comparable divided daily dose of INDERAL tablets. The lower AUCs for the capsules are due to greater hepatic metabolism of propranolol, resulting from the slower rate of absorption of propranolol. Over a twenty-four (24) hour period, blood levels are fairly constant for about twelve (12) hours then decline exponentially.

INDERAL LA should not be considered a simple mg for mg substitute for conventional propranolol and the blood levels achieved do not match (are lower than) those of two to four times daily dosing with the same dose. When changing to INDERAL LA from conventional propranolol, a possible need for retitration upwards should be considered especially to maintain effectiveness at the end of the dosing interval. In most clinical settings, however, such as hypertension or angina where there is little correlation between plasma levels and clinical effect, INDERAL LA has been therapeutically equivalent to the same mg dose of conventional INDERAL as assessed by 24-hour effects on blood pressure and on 24-hour exercise responses of heart rate, systolic pressure and rate pressure product. INDERAL LA can provide effective beta blockade for a 24-hour period.

The mechanism of the antihypertensive effect of INDERAL has not been established. Among the factors that may be involved in contributing to the antihypertensive action are (1) decreased cardiac output, (2) inhibition of renin release by the kidneys, and (3) diminution of tonic sympathetic nerve outflow from vasomotor centers in the brain. Although total peripheral resistance may increase initially, it readjusts to or below the pretreatment level with chronic use. Effects on plasma volume appear to be minor and somewhat variable. INDERAL has been shown to cause a small increase in serum potassium concentration when used in the treatment of hypertensive patients.

In angina pectoris, propranolol generally reduces the oxygen requirement of the heart at any given level of effort by blocking the catecholamine-induced increases in the heart rate, systolic blood pressure, and the velocity and extent of myocardial contraction. Propranolol may increase oxygen requirements by increasing left ventricular fiber length, end diastolic pressure and systolic ejection period. The net physiologic effect of beta-adrenergic blockade is usually advantageous and is manifested during exercise by delayed onset of pain and increased work capacity.

In dosages greater than required for beta blockade, INDERAL also exerts a quinidine-like or anesthetic-like membrane action which affects the cardiac action potential. The significance of the membrane action in the treatment of arrhythmias is uncertain.

The mechanism of the antimigraine effect of propranolol has not been established. Beta-adrenergic receptors have been demonstrated in the pial vessels of the brain.

Beta receptor blockade can be useful in conditions in which, because of pathologic or functional changes, sympathetic activity is detrimental to the patient. But there are also situations in which sympathetic stimulation is vital. For example, in patients with severely damaged hearts, adequate ventricular function is maintained by virtue of sympathetic drive which should be preserved. In the presence of AV block, greater than first degree, beta blockade may prevent the necessary facilitating effect of sympathetic activity on conduction. Beta blockade results in bronchial constriction by interfering with adrenergic bronchodilator activity which should be preserved in patients subject to bronchospasm.

Propranolol is not significantly dialyzable.

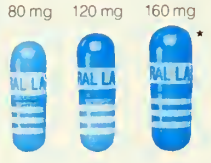
ONCE-DAILY

INDERAL® LA

(PROPRANOLOL HCl)

LONG ACTING CAPSULES

80 mg 120 mg 160 mg



INDICATIONS AND USAGE. Hypertension: INDERAL LA is indicated in the management of hypertension; it may be used alone or used in combination with other antihypertensive agents, particularly a thiazide diuretic. INDERAL LA is not indicated in the management of hypertensive emergencies.

Angina Pectoris Due to Coronary Atherosclerosis: INDERAL LA is indicated for the long-term management of patients with angina pectoris.

Migraine: INDERAL LA is indicated for the prophylaxis of common migraine headache. The efficacy of propranolol in the treatment of a migraine attack that has started has not been established and propranolol is not indicated for such use.

Hypertrophic Subaortic Stenosis: INDERAL LA is useful in the management of hypertrophic subaortic stenosis, especially for treatment of exertional or other stress-induced angina, palpitations, and syncope. INDERAL LA also improves exercise performance. The effectiveness of propranolol hydrochloride in this disease appears to be due to a reduction of the elevated outflow pressure gradient which is exacerbated by beta-receptor stimulation. Clinical improvement may be temporary.

CONTRAINDICATIONS. INDERAL is contraindicated in 1) cardiogenic shock, 2) sinus bradycardia and greater than first degree block, 3) bronchial asthma, 4) congestive heart failure (see WARNINGS) unless the failure is secondary to a tachyarrhythmia treatable with INDERAL.

WARNINGS. CARDIAC FAILURE. Sympathetic stimulation may be a vital component supporting circulatory function in patients with congestive heart failure, and its inhibition by beta blockade may precipitate more severe failure. Although beta blockers should be avoided in overt congestive heart failure, if necessary, they can be used with close follow-up in patients with a history of failure who are well compensated and are receiving digitalis and diuretics. Beta-adrenergic blocking agents do not abolish the inotropic action of digitalis on heart muscle.

IN PATIENTS WITHOUT A HISTORY OF HEART FAILURE, continued use of beta blockers can, in some cases, lead to cardiac failure. Therefore, at the first sign or symptom of heart failure, the patient should be digitalized and/or treated with diuretics, and the response observed closely, or INDERAL should be discontinued (gradually, if possible).

IN PATIENTS WITH ANGINA PECTORIS, there have been reports of exacerbation of angina and, in some cases, myocardial infarction, following abrupt discontinuance of INDERAL therapy. Therefore, when discontinuance of INDERAL is planned the dosage should be gradually reduced over at least a few weeks, and the patient should be cautioned against interruption or cessation of therapy without the physician's advice. If INDERAL therapy is interrupted and exacerbation of angina occurs, it usually is advisable to reinstitute INDERAL therapy and take other measures appropriate for the management of unstable angina pectoris. Since coronary artery disease may be unrecognized, it may be prudent to follow the above advice in patients considered at risk of having occult atherosclerotic heart disease who are given propranolol for other indications.

Nonallergic Bronchospasm (e.g., chronic bronchitis, emphysema) — PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD IN GENERAL NOT RECEIVE BETA BLOCKERS. INDERAL should be administered with caution since it may block bronchodilation produced by endogenous and exogenous catecholamine stimulation of beta receptors.

MAJOR SURGERY. The necessity or desirability of withdrawal of beta-blocking therapy prior to major surgery is controversial. It should be noted, however, that the impaired ability of the heart to respond to reflex adrenergic stimuli may augment the risks of general anesthesia and surgical procedures.

INDERAL (propranolol HCl), like other beta blockers, is a competitive inhibitor of beta-receptor agonists and its effects can be reversed by administration of such agents, e.g., dobutamine or isoproterenol. However, such patients may be subject to protracted severe hypotension. Difficulty in starting and maintaining the heartbeat has also been reported with beta blockers.

DIABETES AND HYPOGLYCEMIA. Beta-adrenergic blockade may prevent the appearance of certain premonitory signs and symptoms (pulse rate and pressure changes) of acute hypoglycemia in labile insulin-dependent diabetes. In these patients, it may be more difficult to adjust the dosage of insulin.

THYROTOXICOSIS. Beta blockade may mask certain clinical signs of hyperthyroidism. Therefore, abrupt withdrawal of propranolol may be followed by an exacerbation of symptoms of hyperthyroidism, including thyroid storm. Propranolol does not distort thyroid function tests.

IN PATIENTS WITH WOLFF-PARKINSON-WHITE SYNDROME, several cases have been reported in which, after propranolol, the tachycardia was replaced by a severe bradycardia requiring a demand pacemaker. In one case this resulted after an initial dose of 5 mg propranolol.

PRECAUTIONS. *General.* Propranolol should be used with caution in patients with impaired hepatic or renal function. INDERAL (propranolol HCl) is not indicated for the treatment of hypertensive emergencies.

Beta-adrenoreceptor blockade can cause reduction of intraocular pressure. Patients should be told that INDERAL may interfere with the glaucoma screening test. Withdrawal may lead to return of increased intraocular pressure.

Clinical Laboratory Tests. Elevated blood urea levels in patients with severe heart disease, elevated serum transaminase, alkaline phosphatase, lactate dehydrogenase.

DRUG INTERACTIONS. Patients receiving catecholamine-depleting drugs such as reserpine should be closely observed if INDERAL is administered. The added catecholamine-blocking action may produce an excessive reduction of resting sympathetic nervous activity which may result in hypotension, marked bradycardia, vertigo, syncopal attacks, or orthostatic hypotension.

Carcinogenesis, Mutagenesis, Impairment of Fertility. Long-term studies in animals have been conducted to evaluate toxic effects and carcinogenic potential. In 18-month studies in both rats and mice, employing doses up to 150 mg/kg/day, there was no evidence of significant drug-induced toxicity. There were no drug-related tumorigenic effects at any of the dosage levels. Reproductive studies in animals did not show any impairment of fertility that was attributable to the drug.

Pregnancy. Pregnancy Category C. INDERAL has been shown to be embryotoxic in animal studies at doses about 10 times greater than the maximum recommended human dose.

There are no adequate and well-controlled studies in pregnant women. INDERAL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. INDERAL is excreted in human milk. Caution should be exercised when INDERAL is administered to a nursing woman.

Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS. Most adverse effects have been mild and transient and have rarely required the withdrawal of therapy.

Cardiovascular. bradycardia, congestive heart failure, intensification of AV block, hypotension, paresthesia of hands, thrombocytopenic purpura, arterial insufficiency, usually of the Raynaud type.

Central Nervous System. lightheadedness, mental depression manifested by insomnia, lassitude, weakness, fatigue, reversible mental depression progressing to catatonia, visual disturbances, hallucinations, an acute reversible syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability, slightly clouded sensorium, and decreased performance on neuropsychometrics.

Gastrointestinal. nausea, vomiting, epigastric distress, abdominal cramping, diarrhea, constipation, mesenteric arterial thrombosis, ischemic colitis.

Allergic. pharyngitis and agranulocytosis, erythematous rash, fever combined with aching and sore throat, laryngospasm and respiratory distress.

Respiratory. bronchospasm.

Hematologic. agranulocytosis, nonthrombocytopenic purpura, thrombocytopenic purpura.

Auto-Immune. In extremely rare instances, systemic lupus erythematosus has been reported.

Miscellaneous. alopecia, LE-like reactions, psoriasiform rashes, dry eyes, male impotence and Peyronie's disease have been reported rarely. Oculomucocutaneous reactions involving the skin, serous membranes and conjunctivae reported for a beta blocker (practolol) have been associated with propranolol.

DOSAGE AND ADMINISTRATION. INDERAL LA provides propranolol hydrochloride in a sustained-release capsule for administration once daily. If patients are switched from INDERAL tablets to INDERAL LA capsules, care should be taken to assure that the desired therapeutic effect is maintained. INDERAL LA should not be considered a simple mg for mg substitute. INDERAL. INDERAL LA has different kinetics and produces lower blood levels. Retitration may be necessary especially to maintain effectiveness at the end of the 24-hour dosing interval.

HYPERTENSION — *Dosage must be individualized.* The usual initial dosage is 80 mg INDERAL LA once daily, whether used alone or added to a diuretic. The dosage may be increased to 120 mg once daily or higher until adequate blood-pressure control is achieved. The usual maintenance dosage is 120 to 160 mg once daily. In some instances a dosage of 640 mg may be required. The time needed for full hypertensive response to a given dosage is variable and may range from a few days to several weeks.

ANGINA PECTORIS — *Dosage must be individualized.* Starting with 80 mg INDERAL LA once daily, dosage should be gradually increased at three to seven day intervals until optimum response is obtained. Although individual patients may respond at any dosage level, the average optimum dosage appears to be 160 mg once daily. In angina pectoris, the value and safety of dosage exceeding 320 mg per day have not been established.

If treatment is to be discontinued, reduce dosage gradually over a period of a few weeks (see WARNINGS).

MIGRAINE — *Dosage must be individualized.* The initial oral dose is 80 mg INDERAL LA once daily. The usual effective dose range is 160-240 mg once daily. The dosage may be increased gradually to achieve optimum migraine prophylaxis. If a satisfactory response is not obtained within four to six weeks after reaching the maximum dose, INDERAL LA therapy should be discontinued. It may be advisable to withdraw the drug gradually over a period of several weeks.

HYPERTROPHIC SUBAORTIC STENOSIS — 80-160 mg INDERAL LA once daily.

PEDIATRIC DOSAGE — At this time the data on the use of the drug in this age group are too limited to permit adequate directions for use.

*The appearance of these capsules is a registered trademark of Ayerst Laboratories.

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PERINATAL INFECTIONS
Frequently Asked Questions

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TELEPHONE CONSULTATION 24 hours a day by a faculty neonatologist has been available at the James Whitcomb Riley Hospital for Children for over 11 years. Questions from pediatricians, obstetricians and family practitioners have enabled us to become familiar with clinical problems and questions that confront the community physician. Here are a few of the questions frequently asked on the "hot line," as well as at continuing medical education conferences, about perinatal infections.

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(Q) Should every infant of a mother whose membranes have been ruptured for more than 24 hours have a spinal tap with cerebrospinal fluid (CSF) culture, a blood culture and a urine culture?

(A) If one or more of the following conditions is present in the history or physical examination, the complete septic work-up should be performed: maternal fever, amnionitis, prematurity, low Apgar scores, respiratory distress, or any other symptom or sign in the mother or baby that would increase the likelihood of neonatal infection.

On the other hand, if the mother has no factors in her peripartum history that would increase the risk of neonatal infection, and the infant is healthy and full-term, then the complete septic work-up is not necessarily indicated. It is reasonable, under these circumstances, to do any one of the following:

(1) Obtain a blood culture from the infant and observe the baby closely for any signs of infection.

(2) Perform a complete blood count (CBC) and differential on the infant as a screening test for infection. If the test is normal, observe the infant closely for any indications of sepsis.

(3) Observe the infant closely in the nursery for any sign of infection without screening tests or cultures. If signs of sepsis are noted, evaluate the infant completely for infection and start parenteral antibiotics.

After all, prolonged rupture of the membranes (PROM) occurs in 5 to 10% of all pregnancies. Ten percent of women with PROM develop clinical amnionitis, defined by maternal fever and foul smelling amniotic fluid containing bacteria by gram stain or culture.[1] Bacteriologically confirmed infection occurs in 1% of the infants delivered of women with PROM alone and in 10% of infants whose mothers

develop clinical amnionitis with PROM.[2] Thus, routinely doing laboratory tests on all infants whose mothers have had membranes ruptured for more than 24 hours would mean performing a large number of tests on healthy, non-infected infants. In addition, the majority of infants with sepsis neonatorum are born to mothers whose membranes have not been ruptured for more than 24 hours.

Despite these two observations, the risk of bacterial infection is increased when membranes have been ruptured for more than 24 hours. This fact, coupled with an additional risk factor such as prematurity, respiratory distress, or clinical amnionitis, would make cultures and parenteral antibiotics appropriate. The case fatality rates for neonatal sepsis range from 20 to 75%; a high index of suspicion is needed to avoid missing cases of systemic neonatal bacterial infection. It is reasonable that non-infected infants will be subjected to invasive procedures and laboratory tests in order to identify and treat infected infants in a ratio of at least 10:1.

The need for urine cultures in infants suspected of early onset (first few days) sepsis is questioned by data presented by Visser.[3] Of 188 sets of blood and urine cultures, there were nine (4.8%) positive blood cultures and three (1.6%) positive urine cultures in 11 infants. Concurrent blood and urine cultures were positive for the same organism in one of these infants. The remaining two positive urine cultures were obtained from infants with negative blood cultures. *Staphylococcus epidermidis* was isolated after suprapubic bladder tap from an infant with hyaline membrane disease; the infant was not treated and made an uneventful recovery. The other positive urine culture, which grew *Escherichia coli*, was isolated from an infant who died of extreme prematurity and pulmonary insufficiency at 40 hours of age. The risk of bowel perforation or other complication as a result of suprapubic aspiration must be balanced against the usefulness of the culture.

(Q) Should a spinal tap be performed in each neonate who is being evaluated for possible sepsis?

(A) As a general rule, a spinal tap should be performed in a neonate as part of an evaluation for possible systemic infection. However, in some clinical situations, it may neither be essential nor appropriate. Such situations include:

(1) Severe respiratory distress during the first few hours of life, when the clinical picture strongly suggests hyaline membrane disease, transient tachypnea or persistent fetal circulation.

(2) The infant's clinical condition is labile and in the clinician's judgment, the lumbar puncture (LP) may further aggravate respiratory problems.

Infection as a cause of respiratory distress in a neonate is difficult to rule out. Lumbar puncture, blood cultures and urine cultures are thus performed frequently on neonates with respiratory distress. This approach has resulted in the performance of LPs in many infants during the first few hours of life, including very low birth weight infants with severe hyaline membrane disease, as well as large term infants with persistent fetal circulation. An LP in these small infants and in infants with severe respiratory distress poses significant risk, including hypoxemia and bradycardia.

Approximately one-third of neonates with septicemia have concurrent meningitis. In a 12-month review of 400 infants with 522 sets of concurrent blood and CSF cultures, 40 episodes of sepsis or meningitis were identified.[4] Organisms were isolated from the blood in 39 instances, and the CSF in 10. One infant had *Escherichia coli* isolated from the CSF but had a negative blood culture. Thus, the majority of neonates with meningitis will have a positive blood culture. Certainly, a lumbar puncture should be performed in infants with a positive blood culture who did not have an LP concurrent with the blood culture. A traumatic tap after antibiotics are begun will make it difficult to rule out a partially treated meningitis.

(Q) Are surface cultures of any significance in evaluating the neonate for possible sepsis?

(A) Surface cultures of the skin, auditory canal, pharynx or gastric aspirate are rarely, if ever, useful as a screening test for infection. Surface cultures should never replace cultures of blood, urine or spinal fluid in high risk infants.

Frequently, we receive a call from a physician with a story somewhat like this: A surface culture of a healthy term infant is obtained shortly after birth because the mother had prolonged rupture of membranes, low-grade fever or history of Group B streptococcal colonization. The infant is now two or three days old, has a normal physical examination, has experienced no problems in the nursery, is feeding well, and is ready to go home. However, the laboratory reports that the surface culture is growing *Group B streptococcus*.

Should the physician send the infant home without other tests or treatment? After all, 5-20% of all mothers are colonized with Group B streptococcus during the third trimester of pregnancy and 50-75% of infants delivered from colonized mothers become carriers. Fortunately, invasive disease develops in only one of 50 to 100 colonized infants.

The questions that remain for the physician who has an infant with a positive surface culture are these: Should the physician perform some other screening tests for infection such as a white blood count or differential? Should the infant be bathed with hexachlorophene or other antiseptic solution? Is treatment with parenteral antibiotics for a short course or oral antibotics appropriate?

No clear cut answers exist for these questions. We know that infants with heavy colonization at birth (positive

cultures from the ear, anus, throat and umbilicus) have an 8% chance of early, invasive infection.[5] But, infants with late onset Group B strep infection often are not found to be colonized at birth. Thus, while surface cultures may be useful as an epidemiologic tool when there is a specific nosocomial infection problem in a nursery, they are not useful as a screening or ancillary test in an individual infant.

(Q) What are the most appropriate laboratory tests in a neonate who has clinical signs of congenital infection?

(A) It depends upon the maternal history and findings on physical examination. Many tests are non-specific but suggest that an infectious process is present. Evaluation of the serum IgM has been suggested as a screening tool for congenital infections; however, the IgM is elevated in only one-third of infants with congenital infections. Liver tests such as serum bilirubin concentration and SGPT also may reflect an inflammatory process. However, there are many non-inflammatory reasons for an elevated serum bilirubin. The SGOT and SGPT are often elevated in a symptomatic infant with congenital infection. However, neither is specific for a particular etiology. A decreased platelet count with petechiae may be suggestive of congenital infection; however, bacterial sepsis, necrotizing enterocolitis, and maternal thrombocytopenia may produce the same test results. CT scans of the head are most often used in infants suspected of having congenital cytomegalovirus (CMV), toxoplasmosis or neonatal herpes. Many cases of congenital CMV and toxoplasmosis have a normal head CT at birth. However, microcephaly combined with the presence of periventricular calcifications make the diagnosis of severe congenital CMV likely. And the presence of diffuse calcification associated with microcephaly on CT would suggest congenital toxoplasmosis.[6]

Ophthalmologic consultation for careful eye examination is sometimes useful in congenital infections. Chorioretinitis is most apt to be detected in congenital toxoplasmosis. Cataracts and cloudy cornea may be detected in congenital rubella. Keratoconjunctivitis may be present in neonatal herpes.[6]

Serologic tests that measure IgG antibody are readily available; however, their correct interpretation is complicated by antibodies normally transmitted from mother to fetus. In uninfected infants born to seropositive mothers, IgG antibodies serially decrease with a half-life of one month and disappear between four and nine months of age. Infected infants have IgG antibody levels that are comparable or greater than their mothers. The levels persist for long periods of time. Thus IgG titers to rubella, CMV, and toxoplasmosis may need simultaneous comparison with titers of maternal sera and specimens obtained later in the first year of life before firm conclusions can be made.

Venereal Disease Research Laboratory test (VDRL) is always appropriate and, if positive, should be followed by quantitative VDRLs and Fluorescent Treponemal Antibody testing.

The IgM titers for toxoplasmosis, CMV and rubella may be useful. However, because of their lack of sensitivity and specificity, they should not be relied upon as the sole means of diagnosis. ELISA methods to detect rubella IgM antibody are considered 67% sensitive in postnatally acquired rubella. No data are available regarding their sensitivity and specificity in infants with congenital rubella.

The IgM immunofluorescent test for CMV (IgM anti CMV) is 76% sensitive but poorly specific since this procedure gave a 21% false-positive rate in a large group of uninfected infants. The IgM portion of the indirect immunofluorescent antibody test for toxoplasmosis is 70% sensitive.[7] If the titer is greater than 1:64, it is suggestive of congenital toxoplasmosis.

The most direct means to diagnose a congenital infection in the neonate is recovery of an agent from body fluids or tissues. Viral isolation of CMV from the urine during the first week of life is virtually diagnostic of congenital infection. Infants who acquire CMV during delivery begin to excrete the virus three to 12 weeks postpartum. Isolation of the herpes virus is necessary for the diagnosis of congenital herpetic infection since antibody titers are generally useless. The herpes virus is most easily isolated from skin lesions if they are present. Cultures from the nasopharynx, conjunctiva and CSF have progressively lower yields. Virus isolation in congenital rubella has limited applicability. Special culture methods are needed and prolonged observation of the cultures is necessary. The diagnosis is better investigated serologically.

In summary, optimal methods for the diagnosis of congenital infection depend upon the most likely organism. "TORCH" titers may be a useful beginning, but cultures and other antibody tests will probably be necessary to confirm the diagnosis.

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Update on Thrombolytic Therapy



ADULT CRITICAL CARE MEDICINE

Methodist Hospital OF INDIANA, INC

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A 58-YEAR-OLD MAN presents to the emergency room with crushing substernal chest pain for two hours. His EKG demonstrates a current of injury in leads V1 to V4; acute anterior myocardial infarction is diagnosed. Twenty-five years ago, this patient would have been admitted to a coronary care unit, and the admitting physician would have anticipated and treated subsequent complications such as ventricular arrhythmia, heart block, and congestive heart failure. In 1987, the admitting physician must choose between more aggressive interventions such as acute thrombolytic therapy or acute angioplasty versus conventional monitoring in a CCU.

As pump failure became known as the primary factor determining prognosis after myocardial infarction, attempts were made to limit the amount of myocardial necrosis. After DeWood reported on the large prevalence of thrombus formation during acute myocardial infarction in 1980,[1] many investigators developed large multicenter trials evaluating thrombolytic therapy. The results of these trials have been optimistic, but the long-term benefits of thrombolytic therapy have been more controversial.

This article will briefly review some of the major thrombolytic trials and discuss which patients are ideal candidates for thrombolytic therapy.

Present Agents

Currently, urokinase and streptokinase are the only two lytic agents available for intravenous therapy approved by the Federal Drug Administration (FDA). Both drugs act not only upon the formed clot within the coronary vessel but also systemically to induce fibrinolysis. Urokinase is an endogenous protease, which is a direct activator of plasminogen. Streptokinase is a non-enzymatic protein isolated from beta-hemolytic streptococci and binds with plasminogen to act as a catalyst in the plasminogen $->$ plasmin reaction.

Because of potential bleeding complications noted with streptokinase and urokinase, more specific thrombolytic agents have been developed that act more selectively within the clot (clot specific). Tissue-type plasminogen activator (t-PA) is the most thoroughly studied clot specific agent and will likely be approved soon by the FDA. T-PA is a direct activator of plasminogen, like urokinase, but t-PA has a weak affinity for plasminogen except when plasminogen is bound to fibrin. Other clot specific agents under investigation include single chain urokinase-type plasminogen activator (scu-PA) and acylated streptokinase-plasminogen complexes.

Complications

Minor bleeding complications from thrombolytic therapy are frequent, occurring in up to 47% of patients. Most are related to hemorrhage around an arterial puncture site. Major complications such as gastrointestinal tract bleeding, hematuria, or hemoptysis are uncommon. Cerebrovascular events are even much less common, occurring in fewer than 1% of patients. Presently, there does not appear to be a significant difference in bleeding complications comparing intravenous streptokinase and t-PA. Gastrointestinal tract bleeding was noted in 6% of the t-PA group and in 10% of the streptokinase group in the Thrombolysis in Myocardial Infarction (TIMI) trial.[2] Because many patients treated with thrombolytic therapy have been placed on heparin after completion of their lytic therapy, the relative role of the thrombolytic vs. heparin in the etiology of bleeding complications is difficult to determine. Less vigorous anticoagulation after thrombolytic therapy may therefore lower the incidence of bleeding complications.

Effectiveness

In our institution, the thrombolytic agents used most commonly are streptokinase and t-PA. In October 1981, the Cardiovascular Section of Methodist Hospital of Indiana, Inc. began a pros-

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pective study evaluating the effect of intercoronary streptokinase in acute myocardial infarction.[3] Reperfusion of the occluded vessel was accomplished in 59% of patients. A 59% reperfusion rate was also found in the western Washington study.[4] The Society for Cardiac Angiography maintained a registry of intracoronary streptokinase between 1981 and 1984 and found a 71% reperfusion rate with 1,029 patients.[5]

Although intracoronary streptokinase is highly effective, a cardiac catheterization laboratory is necessary to administer this therapy. Thrombolytic therapy given via a peripheral intravenous infusion can be administered to more patients and also sooner after the onset of symptoms. Studies using this technique usually permit IV infusion of the thrombolytic agent immediately upon arrival at an Emergency Department and follow initial therapy with cardiac catheterization. In our own intravenous streptokinase trial, a patency rate of 64% was found at angiography. If a 13% incidence of spontaneous patency is assumed, as suggested by DeWood, the reperfusion rate ascribed to thrombolysis is about 51%. A lower reperfusion rate (36%) was seen in the TIMI study; however, the European Cooperative Study had a 55% reperfusion rate.[6]

The reperfusion rate of intravenous t-PA has been found to be greater than intravenous streptokinase and roughly equivalent to intracoronary streptokinase. Methodist Hospital was involved in a multicenter, randomized, placebo-controlled trial evaluating t-PA in acute myocardial infarction. At two hours after t-PA infusion, a patency rate of 84% was observed. The TIMI trial demonstrated a 66% reperfusion rate at 90 minutes post-infusion, while the European Cooperative Study had a 70% reperfusion rate. Presently, Methodist Hospital is participating in a standard dose versus high dose study using t-PA. Preliminary results (17 patients) reveal a patency rate at 90 minutes of 100% using high dose t-PA. Unlike streptokinase, increasing dosages of t-PA appear to increase the perfusion rate although at the expense of less clot specificity of the lytic activity.

TABLE
Patient Selection

A. Inclusion Criteria
1. Acute myocardial infarction diagnosed by:
   a. Typical chest pain for at least 30 minutes and for less than six hours duration. May extend time limit if severe ischemic pain persists beyond six hours.
   b. ST segment elevation of > 0.1 mV measured 0.02 seconds after the J print in one of three locations (in the absence of LBBB):
      i) 2 of the 3 inferior leads (II, III, AVF)
      ii) 2 of the 6 precordial leads (V_1 - V_6)
      iii) leads I and AVL

B. Exclusion Criteria
1. Age > 75.
2. Past or present bleeding diathesis or significant GI bleeding.
3. CVA within six months.
4. Major surgery on internal organs during previous 14 days.
5. Uncontrolled hypertension (diastolic BP > 120).
6. Oral anticoagulation therapy.
7. Recent streptokinase.
8. Prolonged CPR within previous two weeks.
9. Severe head or spine trauma within past six months.
10. Women who are not sterile or not post-menopausal.

Benefits

Perhaps most confusing to the primary care physician is determining which patients presenting with myocardial infarction are candidates for acute lytic therapy. The present inclusion and exclusion criteria for thrombolytic therapy at Methodist Hospital are presented in the *Table*.

Thrombolytic therapy has been shown to improve left ventricular function and reduce the size of myocardial infarction. The Methodist Hospital Streptokinase Research[7] group compared early (24 hours) and late (10-14 days) ejection fractions in reperfused and non-reperfused patients. The mean increases in the reperfused group was 8.4% (39 $->$ 47%), while the non-reperfused group had a mean increase of 3.4% (38% $->$ 42%). Improvements in global ejection fractions have been difficult to demonstrate in many studies. Normally perfused segments of myocardium often become hyperkinetic during acute periods of ischemia resulting in a small change in ejection fraction. Improvements of segmental wall motion have been easier to demonstrate both in anterior and inferior infarcts.[8] By examining cardiac enzyme levels, a decrease in infarct size has been demonstrated in both anterior and inferior infarcts.[9,10] A recent randomized, controlled trial by Simoons[10] suggested a 51% decrease in infarct size if treatment was begun less than one hour after onset of symptoms. This improvement in infarct size was reduced to 13% if treatment was delayed two to four hours.

In the acute infarction, early initiation of therapy means not only less muscle damage but also improved sur-

vival. The GISSI trial[11] from Italy clearly demonstrated an improvement in survival with thrombolytic therapy. This was a large multicenter controlled study with 11,806 patients who received either 1.5 million units of streptokinase intravenously or a placebo. Overall in-hospital mortality was reduced 18% in the streptokinase group. Furthermore, there was a direct relationship between the time therapy was initiated and mortality. Those patients treated later than six hours after onset of symptoms did not have any significant benefit; whereas, patients treated less than one hour after onset of symptoms had a 47% decrease in mortality. This improvement in mortality was evident for both sexes and also in the elderly (> 75 years). Location of infarct is an important factor in determining benefits from thrombolytic therapy. Anterior infarcts in the streptokinase group had an improved survival of 21%. Inferior and lateral infarcts showed a trend toward improved survival, but this was not statistically significant.

In conclusion, thrombolytic therapy has a beneficial effect on infarct size, left ventricular function, and most importantly, mortality. Clearly, early initiation of therapy is crucial to these benefits. Improved left ventricular function and smaller infarct size has been shown in both anterior and inferior infarcts, but an improvement in mortality has not been found in inferior infarcts. This reduced benefit is likely related to the generally smaller size of inferior infarctions. There probably still remains a subgroup of patients with large inferior infarctions whose mortality would improve with lytic therapy. Differentiating this subgroup of large inferior infarctions is very difficult at the onset of an infarction. Also, while a patient's immediate mortality may not be affected, the patient's extended prognosis is directly proportional to remaining left ventricular function.

Future Advances

Although acute intervention in myocardial infarction with thrombolytic therapy has become common, many questions remain unanswered. T-PA will likely become available in the next year, but the correct dosage and duration of therapy have yet to be determined. T-PA has a higher reperfusion rate than intravenous streptokinase, but t-PA's more clot specific activity has not yet produced fewer bleeding complications. Future therapies may involve using multiple lytic agents at smaller dosages to produce successful lysis with less of a sytemic fibroinolytic state. Free radical scavengers such as superoxide dismutase may be used to prevent reperfusion injury to the myocardium once the coronary circulation has been re-established.

Perhaps the most important new question is what treatment should follow successful lytic therapy. Both the western Washington study and the ISAM study have demonstrated that the risk of death after lysis still persists and increases over time.[4,12] Although early thrombolysis probably turns many transmural infarctions into non-transmural infarctions, the high grade atherosclerotic stenosis present in the coronary circulation even after successful thrombolytic therapy has a high propensity to form new clot and reocclude the vessel. Mechanical intervention such as angioplasty and bypass surgery, therefore, will probably be necessary to preserve lytic therapy's improved survival.

The future of thrombolytic therapy in acute myocardial infarction seems assured. As primary care and emergency physicians become more familiar with these agents, thrombolytic therapy will move from major medical centers to smaller community hospitals, benefiting many more patients. Early initiation of therapy, combined with appropriate mechanical intervention, should yield significant long-term benefits in mortality and myocardial function.

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MICROBIOLOGY: The bactericidal activity of ceftriaxone results from inhibition of cell wall synthesis. Ceftriaxone has a high degree of stability in the presence of beta-lactamases, both penicillinases and cephalosporinases, of gram-negative and gram-positive bacteria. Ceftriaxone is usually active against the following microorganisms *in vitro* and in clinical infections (see Indications and Usage):

GRAM-NEGATIVE AEROBES: *Enterobacter aerogenes, Enterobacter cloacae, Escherichia coli, Haemophilus influenzae* (including ampicillin-resistant strains), *H parainfluenzae, Klebsiella* species (including *K pneumoniae*), *Neisseria gonorrhoeae* (including penicillinase and nonpenicillinase producing strains), *Neisseria meningitidis, Proteus mirabilis, Proteus vulgaris, Morganella morganii* and *Serratia marcescens*.

Note: Many strains of the above organisms that are multiply resistant to other antibiotics, e.g., penicillins, cephalosporins and aminoglycosides, are susceptible to ceftriaxone sodium.

Ceftriaxone is also active against many strains of *Pseudomonas aeruginosa*.

GRAM-POSITIVE AEROBES: *Staphylococcus aureus* (including penicillinase-producing strains) and *Staphylococcus epidermidis* (Note: methicillin-resistant staphylococci are resistant to cephalosporins, including ceftriaxone), *Streptococcus pyogenes* (Group A beta-hemolytic streptococci), *Streptococcus agalactiae* (Group B streptococci) and *Streptococcus pneumoniae* (Note: Most strains of enterococci, *Streptococcus faecalis* and Group D streptococci are resistant.)

Ceftriaxone also demonstrates *in vitro* activity against the following microorganisms, although the clinical significance is unknown:

GRAM-NEGATIVE AEROBES: *Citrobacter freundii, Citrobacter diversus, Providencia* species (including *Providencia rettgeri*), *Salmonella* species (including *S typhi*), *Shigella* species and *Acinetobacter calcoaceticus*.

ANAEROBES: *Bacteroides* species, *Clostridium* species (Note: most strains of *C difficile* are resistant).

SUSCEPTIBILITY TESTING: Standard susceptibility disk method. Quantitative methods that require measurement of zone diameters give the most precise estimate of antibiotic susceptibility. One such procedure (Bauer AW, Kirby WMM, Sherris JC, Turck M: Antibiotic Susceptibility Testing by a Standardized Single Disk Method, *Am J Clin Pathol* 45: 493-496, 1966, Standardized Disk Susceptibility Test, *Federal Register* 39: 19182-19184, 1974, National Committee for Clinical Laboratory Standards, Approved Standard—ASM-2, Performance Standards for Antimicrobial Disk Susceptibility Tests, July 1975.) has been recommended for use with disks to test susceptibility to ceftriaxone.

Laboratory results of the standardized single-disk susceptibility test using a 30-mcg ceftriaxone disk should be interpreted according to the following three criteria:

1. Susceptible organisms produce zones of 18 mm or greater, indicating that the tested organism is likely to respond to therapy.
2. Organisms that produce zones of 14 to 17 mm are expected to be susceptible if a high dosage (not to exceed 4 gm per day) is used or if the infection is confined to tissues and fluids (e.g., urine) in which high antibiotic levels are attained.
3. Resistant organisms produce zones of 13 mm or less, indicating that other therapy should be selected.

Organisms should be tested with the ceftriaxone disk, since ceftriaxone has been shown by *in vitro* tests to be active against certain strains found resistant to cephalosporin class disks.

Organisms having zones of less than 18 mm around the cephalothin disk are not necessarily of intermediate susceptibility or resistant to ceftriaxone.

Standardized procedures require use of control organisms. The 30-mcg ceftriaxone disk should give zone diameters between 29 and 35 mm, 22 and 28 mm and 17 and 23 mm for the reference strains *E coli* ATCC 25922, *S aureus* ATCC 25923 and *P aeruginosa* ATCC 27853, respectively.

DILUTION TECHNIQUES: Based on the pharmacokinetic profile of ceftriaxone, a bacterial isolate may be considered susceptible if the MIC value for ceftriaxone is not more than 16 mcg/ml. Organisms are considered resistant to ceftriaxone if the MIC is equal to or greater than 64 mcg/ml. Organisms having an MIC value of less than 64 mcg/ml, but greater than 16 mcg/ml, are expected to be susceptible if a high dosage (not to exceed 4 gm per day) is used or if the infection is confined to tissues and fluids (e.g., urine) in which high antibiotic levels are attained.

E coli ATCC 25922, *S aureus* ATCC 25923 and *P aeruginosa* ATCC 27853 are also the recommended reference strains for controlling ceftriaxone-dilution tests. Greater than 95% of MICs for the *E coli* strain should fall within the range of 0.016 to 0.5 mcg/ml. The range for the *S aureus* strain should be 1 to 2 mcg/ml, while for the *P aeruginosa* strain the range should be 8 to 64 mcg/ml.

INDICATIONS AND USAGE: Rocephin is indicated for the treatment of the following infections when caused by susceptible organisms:

LOWER RESPIRATORY TRACT INFECTIONS caused by *Strep pneumoniae, Streptococcus* species (excluding enterococci), *Staph aureus, H influenzae, H parainfluenzae, Klebsiella* species (including *K pneumoniae*), *E coli, E aerogenes, Proteus mirabilis* and *Serratia marcescens*.

SKIN AND SKIN STRUCTURE INFECTIONS caused by *Staph aureus, Staph epidermidis, Streptococcus* species (excluding enterococci), *E cloacae, Klebsiella* species (including *K pneumoniae*), *Proteus mirabilis* and *Pseudomonas aeruginosa*.

URINARY TRACT INFECTIONS (complicated and uncomplicated) caused by *E coli, Proteus mirabilis, Proteus vulgaris, M morganii* and *Klebsiella* species (including *K pneumoniae*).

UNCOMPLICATED GONORRHEA (cervical/urethral and rectal) caused by *Neisseria gonorrhoeae*, including both penicillinase and nonpenicillinase producing strains.

PELVIC INFLAMMATORY DISEASE caused by *N gonorrhoeae*.

BACTERIAL SEPTICEMIA caused by *Staph aureus, Strep pneumoniae, E coli, H influenzae* and *K pneumoniae*.

BONE AND JOINT INFECTIONS caused by *Staph aureus, Strep pneumoniae, Streptococcus* species (excluding enterococci), *E coli, P mirabilis, K pneumoniae* and *Enterobacter* species.

INTRA-ABDOMINAL INFECTIONS caused by *E coli* and *K pneumoniae*.

MENINGITIS caused by *H influenzae, N meningitidis* and *Strep pneumoniae*. Ceftriaxone has also been used successfully in a limited number of cases of meningitis and shunt infections caused by *Staph epidermidis* and *E coli*.

PROPHYLAXIS: The administration of a single dose of ceftriaxone preoperatively may reduce the incidence of postoperative infections in patients undergoing coronary artery bypass surgery.

Although ceftriaxone has been shown to have been as effective as cefazolin in the prevention of infection following coronary artery bypass surgery, no placebo-controlled trials have been conducted to evaluate any cephalosporin antibiotic in the prevention of infection following coronary artery bypass surgery.

SUSCEPTIBILITY TESTING: Before instituting treatment with Rocephin, appropriate specimens should be obtained for isolation of the causative organism and for determination of its susceptibility to the drug. Therapy may be instituted prior to obtaining results of susceptibility testing.

CONTRAINDICATIONS: Rocephin is contraindicated in patients with known allergy to the cephalosporin class of antibiotics.

WARNINGS: BEFORE THERAPY WITH ROCEPHIN IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEPHALOSPORINS, PENICILLINS OR OTHER DRUGS. THIS PRODUCT SHOULD BE GIVEN CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS. ANTIBIOTICS SHOULD BE ADMINISTERED WITH CAUTION TO ANY PATIENT WHO HAS DEMONSTRATED SOME FORM OF ALLERGY, PARTICULARLY TO DRUGS. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE THE USE OF SUBCUTANEOUS EPINEPHRINE AND OTHER EMERGENCY MEASURES.

Pseudomembranous colitis has been reported with the use of cephalosporins (and other broad-spectrum antibiotics); therefore, it is important to consider its diagnosis in patients who develop diarrhea in association with antibiotic use.

ROCEPHIN® (ceftriaxone sodium/Roche)

Treatment with broad-spectrum antibiotics alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis. Cholestyramine and colestipol resins have been shown to bind to the toxin *in vitro*.

Mild cases of colitis respond to drug discontinuance alone. Moderate to severe cases should be managed with fluid, electrolyte and protein supplementation as indicated.

When the colitis is not relieved by drug discontinuance or when it is severe, oral vancomycin is the treatment of choice for antibiotic-associated pseudomembranous colitis produced by *C difficile*. Other causes of colitis should also be considered.

PRECAUTIONS: *GENERAL*: Although transient elevations of BUN and serum creatinine have been observed, at the recommended dosages, the nephrotoxic potential of Rocephin is similar to that of other cephalosporins.

Ceftriaxone is excreted via both biliary and renal excretion (see Clinical Pharmacology). Therefore, patients with renal failure normally require no adjustment in dosage when usual doses of Rocephin are administered, but concentrations of drug in the serum should be monitored periodically if evidence of accumulation exists, dosage should be decreased accordingly.

Dosage adjustments should not be necessary in patients with hepatic dysfunction, however, in patients with both hepatic dysfunction and significant renal disease, Rocephin dosage should not exceed 2 gm daily without close monitoring of serum concentrations.

Alterations in prothrombin times have occurred rarely in patients treated with Rocephin. Patients with impaired vitamin K synthesis or low vitamin K stores (e.g., chronic hepatic disease and malnutrition) may require monitoring of prothrombin time during Rocephin treatment. Vitamin K administration (10 mg weekly) may be necessary if the prothrombin time is prolonged before or during therapy.

Prolonged use of Rocephin may result in overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Rocephin should be prescribed with caution in individuals with a history of gastrointestinal disease, especially colitis.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY: Carcinogenesis: Considering the maximum duration of treatment and the class of the compound, carcinogenicity studies with ceftriaxone in animals have not been performed. The maximum duration of animal toxicity studies was six months.

Mutagenesis: Genetic toxicology tests included the Ames test, a micronucleus test and a test for chromosomal aberrations in human lymphocytes cultured *in vitro* with ceftriaxone. Ceftriaxone showed no potential for mutagenic activity in these studies.

Impairment of Fertility: Ceftriaxone produced no impairment of fertility when given intravenously to rats at daily doses up to 586 mg/kg/day, approximately 20 times the recommended clinical dose of 2 gm/day.

PREGNANCY: Teratogenic Effects: Pregnancy Category B. Reproductive studies have been performed in mice and rats at doses up to 20 times the usual human dose and have no evidence of embryotoxicity, fetotoxicity or teratogenicity. In primates, no embryotoxicity or teratogenicity was demonstrated at a dose approximately three times the human dose.

There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproductive studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nonteratogenic Effects: In rats, in the Segment I (fertility and general reproduction) and Segment III (perinatal and postnatal) studies with intravenously administered ceftriaxone, no adverse effects were noted on various reproductive parameters during gestation and lactation, including postnatal growth, functional behavior and reproductive ability of the offspring, at doses of 586 mg/kg/day or less.

NURSING MOTHERS: Low concentrations of ceftriaxone are excreted in human milk. Caution should be exercised when Rocephin is administered to a nursing woman.

PEDIATRIC USE: Safety and effectiveness of Rocephin in neonates, infants and children have been established for the dosages described in the Dosage and Administration section.

ADVERSE REACTIONS: Rocephin is generally well tolerated. In clinical trials, the following adverse reactions, which were considered to be related to Rocephin therapy or of uncertain etiology, were observed:

LOCAL REACTIONS—pain, induration or tenderness at the site of injection (1%). Less frequently reported (less than 1%) was phlebitis after IV administration.

HYPERSENSITIVITY—rash (1.7%). Less frequently reported (less than 1%) were pruritus, fever or chills.

HEMATOLOGIC—eosinophilia (6%), thrombocytosis (5.1%) and leukopenia (2.1%). Less frequently reported (less than 1%) were anemia, neutropenia, lymphopenia, thrombocytopenia and prolongation of the prothrombin time.

GASTROINTESTINAL—diarrhea (2.7%). Less frequently reported (less than 1%) were nausea or vomiting and dysgeusia.

HEPATIC—elevations of SGOT (3.1%) or SGPT (3.3%). Less frequently reported (less than 1%) were elevations of alkaline phosphatase and bilirubin.

RENAL—elevations of the BUN (1.2%). Less frequently reported (less than 1%) were elevations of creatinine and the presence of casts in the urine.

CENTRAL NERVOUS SYSTEM—headache or dizziness were reported occasionally (less than 1%).

GENITOURINARY—moniliasis or vaginitis were reported occasionally (less than 1%).

MISCELLANEOUS—diaphoresis and flushing were reported occasionally (less than 1%).

Other rarely observed adverse reactions (less than 0.1%) include leukocytosis, lymphocytosis, monocytosis, basophilia, a decrease in the prothrombin time, jaundice, glycosuria, hematuria, bronchospasm, serum sickness, abdominal pain, colitis, flatulence, dyspepsia, palpitations and epistaxis.

DOSAGE AND ADMINISTRATION: Rocephin may be administered intravenously or intramuscularly. The usual adult daily dose is 1 to 2 gm given once a day (or in equally divided doses twice a day) depending on the type and severity of the infection. The total daily dose should not exceed 4 grams.

For the treatment of serious miscellaneous infections in children other than meningitis, the recommended total daily dose is 50 to 75 mg/kg (not to exceed 2 grams), given in divided doses every 12 hours. Generally, Rocephin therapy should be continued for at least two days after the signs and symptoms of infection have disappeared. The usual duration is 4 to 14 days; in complicated infections longer therapy may be required.

In the treatment of meningitis, a daily dose of 100 mg/kg (not to exceed 4 grams), given in divided doses every 12 hours, should be administered with or without a loading dose of 75 mg/kg.

For the treatment of uncomplicated gonococcal infections, a single intramuscular dose of 250 mg is recommended.

For preoperative use (surgical prophylaxis), a single dose of 1 gm administered ½ to 2 hours before surgery is recommended.

When treating infections caused by *Streptococcus pyogenes*, therapy should be continued for at least ten days.

No dosage adjustment is necessary for patients with impairment of renal or hepatic function, however, blood levels should be monitored in patients with severe renal impairment (e.g., dialysis patients) and in patients with both renal and hepatic dysfunctions.

HOW SUPPLIED: Rocephin (ceftriaxone sodium/Roche) is supplied as a sterile crystalline powder in glass vials and piggyback bottles. The following packages are available:

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Vials containing 2 gm equivalent of ceftriaxone. Boxes of 10 (NDC 0004-1965-01)

Piggyback bottles containing 2 gm equivalent of ceftriaxone. Boxes of 10 (NDC 0004-1965-03)

Bulk pharmacy containers, containing 10 gm equivalent of ceftriaxone. Boxes of 1 (NDC 0004-1971-01)

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Hemorrhoidectomy in a Hemophiliac with Factor VIII Inhibitors

MAGARAL S. MURALI, M.D.
RAMA M. JAGER, M.D., Ph.D.
Indianapolis

WITH THE AVAILABILITY of clotting factor concentrates, many surgical procedures in hemophiliacs can now be performed with a reasonable degree of safety. However, when the surgical wound heals or by second intention as after a hemorrhoidectomy, and when a hemophiliac develops factor VIII inhibitors, the risk of postoperative bleeding may be high. We present our experience of successful management of hemorrhoidectomy with epsilon amino caproic acid (EACA) in a hemophiliac who developed factor VIII inhibitors during the immediate postoperative period.

Case Report

A 38-year-old man with classic hemophilia A was admitted for surgical hemorrhoidectomy because of chronic anorectal bleeding of two years duration. The rectal bleeding was severe enough to require multiple blood transfusions. The patient had had many episodes of post traumatic and intraarticular bleeding since his childhood, but never required prophylactic factor VIII infusions. The patient's rectal bleeding was confirmed to be emanating from both the internal and subanodermal component of his external hemorrhoids; therefore, it was felt not to be amenable to Barron's band ligation or sclerotherapy. His hemoglobin on admission was 10.4 g%, platelets - 332,000/ml, and fibrinogen - 565mg/dl. Prothrombin and thrombin times were normal but partial thromboplastin time was 80 seconds (control 28 seconds). Factor VIII:C level on admission was less than 1%.

Before the operation, the patient was transfused with factor VIII concentrates at a dose of 50 units/kg. With the preoperative factor VIII level of 123%, internal and external hemorrhoidectomy was done without any transoperative complications; the operative blood loss was 50 ml. Postoperatively, factor VIII transfusions were given every 12 hours as needed to maintain factor VIII at hemostatic levels. Beginning on the fourth postoperative day, the patient started to have an increasing amount of rectal bleeding from the surgical wound and factor VIII levels started to decrease despite the frequent and increasing doses of Factor VIII supplements.

Factor VIII inhibitor levels were determined on the 11th postoperative day and found to be less than three Bethesda units. On the 17th postoperative day, the patient had massive rectal bleeding and developed hemorrhagic shock requiring massive transfusions of blood, crystalloid fluids and factor VIII supplements. Because of continued rectal bleeding despite these measures, we initiated treatment with intravenous epsilon amino caproic acid (EACA) with a loading dose of 4 g as an intravenous bolus and then a continuous intravenous infusion of 1 g/hr. Within four hours after the initiation of EACA infusions, the patient's rectal bleeding markedly decreased and over the next few days the need for factor VIII supplements to maintain anorectal hemostasis also decreased. The intravenous EACA was continued from the 17th through the 22nd postoperative day. Oral EACA was started on the 22nd postoperative day, prior to his discharge from the hospital. The patient's anorectal wounds healed with no further complications and he had no further rectal bleeding during a follow-up period of over two years.

Discussion

The rectal bleeding in this patient was diagnosed to be emanating from the hemorrhoids and was severe enough to require frequent packed red blood cell transfusions for almost two years before the decision was made to control his rectal bleeding by hemorrhoidectomy. Nonsurgical management by band ligation or other mucosal fixation techniques were felt to be inadequate to control the problem since the rectal bleeding appeared to stem from both the internal hemorrhoids and external hemorrhoids. Surgical hemorrhoidectomy is not the ideal treatment of hemorrhoids in a hemophiliac and should only be done when all other methods have failed.

Principles of management for hemophiliacs during and after surgical procedures are fairly well established;[1] replacement of factor VIII concentrates are considered the mainstay of hemostatic management in hemophiliacs. However, management of a hemophiliac with factor VIII inhibitors can be formidable. Development of inhibitors became evident in our patient when massive doses of factor VIII concentrates failed to raise the plasma level of factor VIII over 5%, and this was confirmed by identification of three Bethesda units of factor VIII

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inhibitors.

EACA is being used to control postoperative bleeding in hemophiliacs undergoing dental and oral surgical procedures because of the protective effect of EACA on the primary clot through antifibrinolysis.[2]

Activated prothrombin complex (Autoplex®) may be used to control bleeding in hemophiliacs;[3] however, we decided against this agent for our patient because his factor VIII inhibitor levels were not high enough to risk induction of disseminated intravascular coagulation. Also, Autoplex was not available at the time our patient developed massive rectal bleeding leading to systemic arterial hypotension.

The cessation of bleeding after initiation of EACA infusion and decreased requirements of factor VIII infusions to maintain adequate levels suggest the hemostatic efficacy of EACA. Although the use of EACA has been recommended for routine use in all hemophiliacs undergoing oral surgery,[4] the various thrombotic consequences of EACA administration should be considered before deciding on its hemostatic use for patients undergoing other procedures.

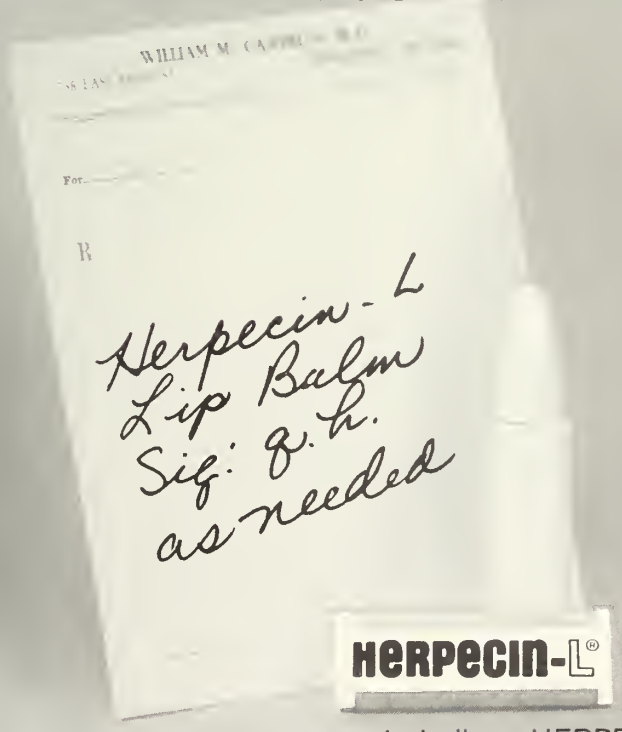
Summary

Successful management of posthemorrhoidectomy bleeding in a hemophiliac who developed factor VIII inhibitors in the postoperative period by use of epsilon amino caproic acid is reported.

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Retroperitoneal Fibrosis and Sclerosing Mediastinitis

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JOHN P. MORAN JR., M.D.
JAMES C. DILLON, M.D.
JAMES A. MADURA, M.D.
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FIGURE 1: Chest x-ray on 3/83 shows mediastinal widening.

RETROPERITONEAL FIBROSIS (RPF) is a rare and poorly understood process that creates havoc with retroperitoneal structures, such as the ureters, vena cava, and retroperitoneal portions of intestine. Its recognition reached a peak when an association was noted with the use of methysergide for the prevention of migraine headaches. However, the process was seen before this drug, and has continued to occur after the drug has been largely abandoned.

Even more unusual has been a similar process occurring in the mediastinum, with or without the retroperitoneal process. Various explanations have been given for the onset of the disease, including histoplasmosis,[1] other infections,[2] malignancies, autoimmune and collagen diseases, as well as the previously mentioned drug reactions.

More perplexing than the etiology of RPF is the treatment. Steroids, antimetabolites, various anti-inflammatory agents, and irradiation have all been used with little effect. Surgical approaches generally have fallen into the category of "putting out brush fires," in both the chest and abdomen. The major threat to life has been ureteral entrapment and renal failure, but the mediastinal fibrosis has been equally worrisome, because of occlusion of the superior vena cava. Of the few cases of combined mediastinal and retroperitoneal disease reported in the world's literature, no support can be found for any specific single or combined modality of treatment. This paper presents such a case and describes its current treatment and prognosis, as well as a review of the pertinent literature on the topic.

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Case Presentation

The patient is a 46-year-old white man who originally presented to the Indiana University Medical Center in January 1983. His presenting symptoms were a swollen neck, engorged jugular veins and dusky discoloration of his upper thorax. His local physician had made the diagnosis of superior vena cava syndrome by obtaining a venogram showing a totally occluded superior vena cava. No etiology for this process was discovered at his local hospital and therefore he was referred for further diagnostic work-up and therapy.

At I.U.M.C., his physical examination demonstrated facial plethora, dilated jugular veins, neck "fullness," and a few small palpable cervical nodes. His chest x-ray showed mediastinal widening (*Fig. 1*). Sputum cytology was negative for malignancy. Cervical lymph nodes biopsy demon-

strated only reactive hyperplasia. Bone marrow aspiration suggested extramedullary hematopoeisis, but no malignant infiltration.

An infectious disease evaluation was negative for tuberculosis, histoplasmosis, blastomycosis, aspergillosis, and coccidiomycosis. The serological test for syphilis was also negative. A collagen vascular work-up was negative for the rheumatoid factor and ANA, but the L-E preparation was positive.

Chest CT confirmed the vena caval occlusion, as well as dilated azygous and hemiazygous veins, and extensive superficial thoraco-abdominal venous collaterals. The cardiac echocardiogram and ECG were both unremarkable.

His past medical history was positive for previous left lower lobectomy for bronchiectasis at age 20; excision of a left neck cyst at age 25; pneumonia at age 28; glomerulonephritis at age 33; and treatment of "arthritis" with non-steroidal agents within the past eight to 10 years.

He was discharged with a diagnosis of idiopathic superior vena caval syndrome on no specific treatment.

Two months later, his symptoms worsened and he returned. He underwent a right anterior thoracotomy and a large firm mass was identified, tightly adherent to the right anterolateral aspect of the trachea. It was felt to be unresectable, and therefore only biopsies were done. (*Fig. 4*) Internal mammary and paratracheal nodes were also sent for histologic examination and cultures. The superior vena cava was identified and thought to be compressible. Aerobic, fungal, and AFB cultures were all negative, while a few proprionibacterium acnes grew anaerobically. Postoperatively, he did well except for a left upper extremity thrombophlebitis for which he was anticoagulated. The pathology report was idiopathic fibrosing mediastinitis.

He was discharged on Coumadin, and did well for the next three years. Eventually, the Coumadin was stopped without event.



FIGURE 2: Hypotonic duodenography, 6/86. The third and fourth portions of the duodenum show compression and narrowing by an extrinsic mass.

In June 1986, he was readmitted to I.U.M.C., this time complaining of bilious vomiting for one month. In addition, he had right upper quadrant discomfort, fatigue and a 10-pound weight loss. The superior vena caval symptoms were not any worse at this time. His physical exam showed only some RUQ tenderness and the previously observed thoracoabdominal venous dilitation. Abnormal lab values were: alkaline phosphatase-308u, BUN-57mg% and creatinine-2.8mg%. His work-up included: upper GI endoscopy, which showed extrinsic narrowing of the 3rd and 4th portions of the duodenum; hypotonic duodenography, which showed the same (*Fig. 2*); abdominal CT, which showed a thickened upper abdominal retroperitoneum and left hydronephrosis; and finally, retrograde pyelography, which showed a left UPJ stenosis and left pelvic and calyceal dilatation, with medial deviation of the right ureter (*Fig. 3*).

Because of his duodenal obstruction, he was taken to the operating room where the retroperitoneum, the small bowel and colonic mesenteries were observed to be encased by a dense fibrotic process. Biopsies were taken, and an antecolic posterior gastrojejunostomy was done because the fibrotic process prevented sufficient mobilization for a duodenojejunostomy. No vagotomy was performed because dense adhesions with dilated collateral vessels were present in the left upper quadrant.

The retroperitoneal mass biopsies demonstrated a fibrotic and inflam-



FIGURE 3: Retrograde pyelography, 6/86. There is medial deviation of the right ureter and some evidence of uretero-pelvic junction obstruction on the left.

matory mass, similar to his previous mediastinal process (*Fig. 5*). Postoperatively, he did well and 10 days later underwent left ureteropelvic junction lysis with internal stenting and external wrapping with perinephric fat. Several days later the right ureter was intubated with a permanent double pig-tailed stent. He was subsequently discharged, eating a regular diet and taking cimetidine.

Discussion

Retroperitoneal fibrosis and sclerosing mediastinitis are similar disease processes. At present, nearly 500 cases of retroperitoneal fibrosis have been reported.[3] The mediastinal form has been reported less often. The combined process, as illustrated in the case presentation, has been documented only eight times previously. The disease was originally described by Albarran in 1905,[4] but was not fully appreciated until 1948, when Ormond described two cases of ureteral obstruction as a result of this fibrous obliteration.[5] Sclerosing mediastinitis was alluded to by Hunter in 1757 as a cause of superior vena caval obstruction.[1]

Both varieties of the disease present in later life, with 54% of the cases being reported in the 5th to 6th decades of life. There is a male predominance of 2:1 in the retroperitoneal form,[3] but no gender difference in the mediastinal form. No epidemiological correlations are noted with reference to race, geographical location, occupation or specific lifestyles.

The etiology of this process is poorly understood. The only known provocative agent has been methysergide, and large series have shown that one percent of those taking this drug will be affected.[6] Koep's collective review of 481 cases showed 12% of patients to have taken methysergide, while 68% had no causative agent whatsoever identified.[3] In addition, in Koep's collective review, 8% of the patients had associated malignancies.[3] While this may be purely coincidental, perhaps some hyper-reactive response to specific stimuli, such as tumors, drugs or infectious agents may be involved.

The mediastinal process, in the past, has been attributed to tuberculosis, syphilis, histoplasmosis, collagen vascular diseases and even trauma,[1,2,7] However, like the retroperitoneal process, most cases are truly idiopathic. The dense fibrotic and inflammatory nature of the response leads to speculation that the affected individuals have an exaggerated response to *any* insult, be it infectious, neoplastic, traumatic or drug mediated. It has been likened to keloid formation, although no correlation has been made between keloid-forming patients and this disease.[8]

The clinical presentation of the abdominal form of the disease is most frequently related to ureteral obstruction. It is reported to occur in 75% of patients.[9] Symptoms related to the process include back, flank, and abdominal pain, as well as symptoms of azotemia and uremia.

Distal venous occlusion may lead to leg edema and pain. The gastrointestinal tract has been infrequently

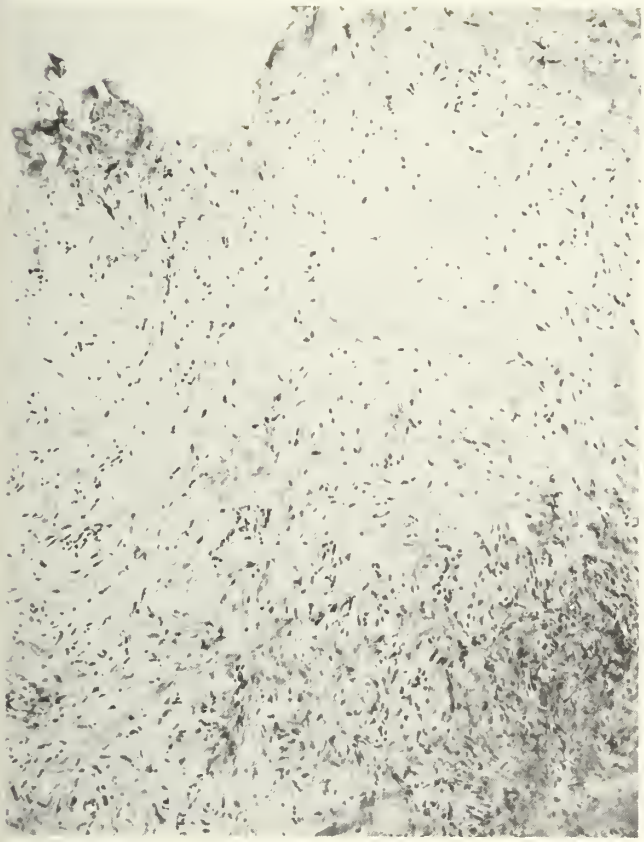


FIGURE 4: Biopsy of paratracheal mass, 1983. Demonstrates the dense fibrosis with no evidence of neoplasia or granulomatous process. (Magnification = 100X)



FIGURE 5: Biopsy of retroperitoneal fibrous plaque that was compressing the duodenum. Dense fibrosis is present, along with some inflammatory infiltrate. (Magnification = 100X)

involved, but compression of the retroperitoneal duodenum leads to signs of high small bowel obstruction, while involvement of the pelvic colon would lead to a picture of chronic distal colic obstruction. The mediastinal form of the disease presents most frequently as superior vena caval obstruction with dilated cervical and brachial veins, facial and upper extremity edema, headache, dizziness, and mental lethargy. These symptoms usually diminish as collateral venous circulation develops.[10] Hemoptysis may present, but tracheo-bronchial stenosis and constriction usually do not occur because of the cartilagenous support of these structures.[11] Thrombosis of the superior vena cava may ensue, and pulmonary embolization may result. Finally, esophageal varices and upper gastrointestinal bleeding may result from involvement of the supra-hepatic inferior vena cava.

Pathology—Grossly, the process appears as a dense, hard "plaque," with poorly defined boundaries. It can be densely adherent to various vital structures and may be nearly impossible to dissect away. In the abdomen it can extend from the lower diaphragm to the sacral promontory and, as mentioned, usually envelops the ureters and displaces them medially. In the mediastinum, the mass grossly appears the same and is usually adherent to the tracheo-bronchial tree and the great vessels. Initially, it may be misdiagnosed as a widespread malignant process until the biopsy reports are returned.[10]

Microscopically, the tissue appears as a diffuse, monotonous, fibrocollagenous stroma with varying degrees of inflammatory infiltrate (*Figs. 4,5*). Adequate and varied biopsy samples are necessary to distinguish this process from a severe desmoplastic reaction surrounding a neoplastic process.

Diagnosis—The history and physical exam are important in making this diagnosis. Ureteral or superior vena caval obstructive signs and symptoms should alert one to this diagnosis. Laboratory studies are of minimal help, but an elevated sedimentation rate, or increased BUN and creatinine may be present. A positive L-E prep has been

reported in several cases in the literature, as well as the present case. Its significance remains unknown, and none of the involved patients has demonstrated any other evidence of systemic lupus erythematosis.

Radiologically, a chest x-ray will usually show a widened mediastinum or evidence of dilated azygous veins. A superior vena cavagram will demonstrate either compression or total obstruction of the superior vena cava. Later, prominent collaterals will be visible. In the retroperitoneal process, an IVP will be nearly pathognomonic, showing medial deviation of the ureters, and eventually UPJ obstruction and hydronephrosis. A CT scan may demonstrate the homogeneous fibrotic process, but even more importantly, will rule out the lymphadenopathy seen in lymphomas and other malignancies. The only true method of diagnosis is by biopsy and histopathologic investigation.

The differential diagnosis should include infections such as tuberculosis and chronic fungal processes, lymphomas and other malignancies, trauma, and the collagen vascular diseases.

Treatment—Medical therapy of this disease has been largely unsuccessful. Corticosteroids have been used extensively, but seem to be effective only in the early phases of the disease or if the chronic process reactivates.[7,12] Once the mass becomes densely fibrotic and contracted, steroids seem to be ineffective.

Surgical therapy is reserved mainly for obstructive and potentially life-threatening situations. No extensive dissection of the mediastinal process should be attempted, since collateral veins will temper the SVC symptoms to a large degree. However, a thoracotomy is usually indicated in the mediastinal process to rule out a neoplastic or infectious etiology.

With ureteral obstruction, it is important for the urologist to "lyse" the ureters from within the fibrotic plaque and either wrap them with omental or peritoneal fat, or completely intraperitonealize the ureters to prevent further envelopment.[13] If the ureters cannot be freed, internal stents should be placed to restore as much renal function as possible.

If the duodenum is involved, it is usually impossible to safely remove the fibrous reaction or to transpose the bowel to a safer location. Generally, a bypass of the involved segment is simpler and will provide for long-term relief of symptoms. Again, several deep biopsies are necessary to establish the true diagnosis.[14]

In general, unless there is impending ureteral, vascular or gastrointestinal compression and obstruction, only supportive measures are necessary. Once the diagnosis is established, periodic evaluation of renal function by IVP and serum chemistry is mandatory.

The overall prognosis in this disease appears to be quite good, if renal function is maintained and no other serious disease processes are found. The overall mortality of the reported cases is about 10% and almost all of the deaths were related to renal failure and its subsequent problems.[3]

Summary

Retroperitoneal and mediastinal fibrosis are rare and poorly understood processes. Generally, they are idiopathic in origin, but methysergide, chronic infections, neoplasms, trauma and collagen vascular diseases have all been implicated in the etiology. Symptoms are related to compression of vital structures by the fibrosing process, with ureteral occlusion and superior vena caval obstruction the predominant clinical problems.

Therapy with steroids may be of limited benefit early in the course of the disease. Surgical intervention is indicated for biopsy and diagnosis, as well as alleviating the obstruction of the ureters by lysis and/or internal stenting. Should the bowel become involved with this process, resection or bypass of the involved portion may become necessary.

The prognosis of the disease is good as long as renal function is preserved. Long-term survival appears to be about 90% in collected series from the world's literature.

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Prevent genital herpes recurrences month after month with daily therapy.

(In controlled studies, recurrences were totally prevented for 4 to 6 months in up to 75% of patients.)

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Coping with genital herpes is rarely easy. For some, the worst part is the pain and discomfort of frequent attacks—month after month, year after year. For others, the emotional burden presents a more difficult problem, leading to social isolation, anxiety, and diminished self-esteem.

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The physical and emotio difficulties posed by genita herpes are unique for each patient. The frequency and severity of recurrent episod as well as the emotional impact of the disease, shoul be considered when selecti daily therapy with ZOVIRA CAPSULES.

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Prevent recurrences month after month*

ZOVIRAX® (acyclovir) CAPSULES

Brief Summary

INDICATIONS AND USAGE: Zovirax Capsules are indicated for the treatment of initial episodes and the management of recurrent episodes of genital herpes in certain patients.

The severity of disease is variable depending upon the immune status of the patient, the frequency and duration of episodes, and the degree of cutaneous or systemic involvement. These factors should determine patient management, which may include symptomatic support and counseling only, or the institution of specific therapy. The physical, emotional and psychosocial difficulties posed by herpes infections as well as the degree of debilitation, particularly in immunocompromised patients, are unique for each patient, and the physician should determine therapeutic alternatives based on his or her understanding of the individual patient's needs. Thus Zovirax Capsules are not appropriate in treating all genital herpes infections. The following guidelines may be useful in weighing the benefit/risk considerations in specific disease categories:

First Episodes (primary and nonprimary infections — commonly known as initial genital herpes):

Double-blind, placebo-controlled studies have demonstrated that orally administered Zovirax significantly reduced the duration of acute infection (detection of virus in lesions by tissue culture) and lesion healing. The duration of pain and new lesion formation was decreased in some patient groups. The promptness of initiation of therapy and/or the patient's prior exposure to Herpes simplex virus may influence the degree of benefit from therapy. Patients with mild disease may derive less benefit than those with more severe episodes. In patients with extremely severe episodes, in which prostration, central nervous system involvement, urinary retention or inability to take oral medication require hospitalization and more aggressive management, therapy may be best initiated with intravenous Zovirax.

Recurrent Episodes:

Double-blind, placebo-controlled studies in patients with frequent recurrences (6 or more episodes per year) have shown that Zovirax Capsules given for 4 to 6 months prevented or reduced the frequency and/or severity of recurrences in greater than 95% of patients. Clinical recurrences were prevented in 40 to 75% of patients. Some patients experienced increased severity of the first episode following cessation of therapy; the severity of subsequent episodes and the effect on the natural history of the disease are still under study.

The safety and efficacy of orally administered acyclovir in the suppression of frequent episodes of genital herpes have been established only for up to 6 months. Chronic suppressive therapy is most appropriate when, in the judgement of the physician, the benefits of such a regimen outweigh known or potential adverse effects. In general, Zovirax Capsules should not be used for the suppression of recurrent disease in mildly affected patients. Unanswered questions concerning the human relevance of *in vitro* mutagenicity studies and reproductive toxicity studies in animals given very high doses of acyclovir for short periods (see Carcinogenesis, Mutagenesis, Impairment of Fertility) should be borne in mind when designing long-term management for individual patients. Discussion of these issues with patients will provide them the opportunity to weigh the potential for toxicity against the severity of their disease. Thus, this regimen should be considered only for appropriate patients and only for six months until the results of ongoing studies allow a more precise evaluation of the benefit/risk assessment of prolonged therapy.

Limited studies have shown that there are certain patients for whom intermittent short-term treatment of recurrent episodes is effective. This approach may be more appropriate than a suppressive regimen in patients with infrequent recurrences.

Immunocompromised patients with recurrent herpes infections can be treated with either intermittent or chronic suppressive therapy. Clinically significant resistance, although rare, is more likely to be seen with prolonged or repeated therapy in severely immunocompromised patients with active lesions.

CONTRAINDICATIONS: Zovirax Capsules are contraindicated for patients who develop hypersensitivity or intolerance to the components of the formulation.

WARNINGS: Zovirax Capsules are intended for oral ingestion only.

PRECAUTIONS: General: Zovirax has caused decreased spermatogenesis at high doses in some animals and mutagenesis in some acute studies at high concentrations of drug (see PRECAUTIONS — Carcinogenesis, Mutagenesis, Impairment of Fertility). The recommended dosage and length of treatment should not be exceeded (see DOSAGE AND ADMINISTRATION).

Exposure of Herpes simplex isolates to acyclovir *in vitro* can lead to the emergence of less sensitive viruses. The possibility of the appearance of less sensitive viruses in man must be borne in mind when treating patients. The relationship between the *in vitro* sensitivity of Herpes simplex virus to acyclovir and clinical response to therapy has yet to be established.

Because of the possibility that less sensitive virus may be selected in patients who are receiving acyclovir, all patients should be advised to take particular care to avoid potential transmission of virus if active lesions are present while they are on therapy. In severely immunocompromised patients, the physician should be aware that prolonged or repeated courses of acyclovir may result in selection of resistant viruses which may not fully respond to continued acyclovir therapy.

Drug Interactions: Co-administration of probenecid with intravenous acyclovir has been shown to increase the mean half-life and the area under the concentration-time curve. Urinary excretion and renal clearance were correspondingly reduced.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Acyclovir was tested in lifetime bioassays in rats and mice at single daily doses of 50, 150 and 450 mg/kg given by gavage. There was no statistically significant difference in the incidence of tumors between treated and control animals, nor did acyclovir shorten the latency of tumors. In 2 *in vitro* cell transformation assays, used to provide preliminary assessment of potential oncogenicity in advance of these more definitive life-time bioassays in rodents, conflicting results were obtained. Acyclovir was positive at the highest dose used in one system and the resulting morphologically transformed cells formed tumors when inoculated into immunosuppressed, syngeneic, weanling mice. Acyclovir was negative in another transformation system considered less sensitive.

In acute studies, there was an increase, not statistically significant, in the incidence of chromosomal damage at maximum tolerated parenteral doses of 100 mg/kg acyclovir in rats but not Chinese hamsters; higher doses of 500 and 1000 mg/kg were clastogenic in Chinese hamsters. In addition, no activity was found after 5 days dosing in a dominant lethal study in mice. In 6 of 11 microbial and mammalian cell assays, no evidence of mutagenicity was observed. At 3 loci in a Chinese hamster ovary cell line, the results were inconclusive. In 2 mammalian cell assays (human lymphocytes and L5178Y mouse lymphoma cells *in vitro*), positive responses for mutagenicity and chromosomal damage occurred, but only at concentrations at least 400 times the acyclovir plasma levels achieved in man.

Acyclovir has not been shown to impair fertility or reproduction in mice (450 mg/kg/day, p.o.) or in rats (25 mg/kg/day, s.c.). At 50 mg/kg/day s.c. in the rat, there was a statistically significant increase in post-implantation loss, but no concomitant decrease in litter size. In female rabbits treated subcutaneously with acyclovir subsequent to mating, there was a statistically significant decrease in implantation efficiency but no concomitant decrease in litter size at a dose of 50 mg/kg/day. No effect upon implantation efficiency was observed when the same dose was administered intravenously. In a rat peri- and postnatal study at 50 mg/kg/day s.c., there was a statistically significant decrease in the group mean numbers of corpora lutea, total implantation sites and live fetuses in the F_1 generation. Although not statistically significant, there was also a dose related decrease in group mean numbers of live fetuses and implantation sites at 12.5 mg/kg/day and 25 mg/kg/day, s.c. The intravenous administration of 100 mg/kg/day, a dose known to cause obstructive nephropathy in rabbits, caused a significant increase in fetal resorptions and a corresponding decrease in litter size. However, at a maximum tolerated intravenous dose of 50 mg/kg/day in rabbits, there were no drug-related reproductive effects.

Intraperitoneal doses of 320 or 80 mg/kg/day acyclovir given to rats for 1 and 6 months, respectively, caused testicular atrophy. Testicular atrophy was persistent through the 4-week postdose recovery phase after 320 mg/kg/day; some evidence of recovery of sperm production was evident 30 days postdose. Intravenous doses of 100 and 200 mg/kg/day acyclovir given to dogs for 31 days caused aspermatogenesis. Testicles were normal in dogs given 50 mg/kg/day, i.v. for one month.

Pregnancy: ***Teratogenic Effects:*** Pregnancy Category C. Acyclovir was not teratogenic in the mouse (450 mg/kg/day, p.o.), rat (50 mg/kg/day, s.c.) or rabbit (50 mg/kg/day, s.c. and i.v.). There are no adequate and well-controlled studies in pregnant women. Acyclovir should not be used during pregnancy unless the potential benefit justifies the potential risk to the fetus. Although acyclovir was not teratogenic in animal studies,. the drug's potential for causing chromosome breaks at high concentration should be taken into consideration in making this determination.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Zovirax is administered to a nursing woman. In nursing mothers, consideration should be given to not using acyclovir treatment or discontinuing breastfeeding.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS — Short-Term Administration: The most frequent adverse reactions reported during clinical trials were nausea and/or vomiting in 8 of 298 patient treatments (2.7%) and headache in 2 of 298 (0.6%). Less frequent adverse reactions, each of which occurred in 1 of 298 patient treatments (0.3%), included diarrhea, dizziness, anorexia, fatigue, edema, skin rash, leg pain, inguinal adenopathy, medication taste and sore throat.

Long-Term Administration: The most frequent adverse reactions reported in studies of daily therapy for 3 to 6 months were headache in 33 of 251 patients (13.1%), diarrhea in 22 of 251 (8.8%), nausea and/or vomiting in 20 of 251 (8.0%), vertigo in 9 of 251 (3.6%), and arthralgia in 9 of 251 (3.6%). Less frequent adverse reactions, each of which occurred in less than 3% of the 251 patients (see number of patients in parentheses), included skin rash (7), insomnia (4), fatigue (7), fever (4), palpitations (1), sore throat (2), superficial thrombophlebitis (1), muscle cramps (2), pars planitis (1), menstrual abnormality (4), acne (3), lymphadenopathy (2), irritability (1), accelerated hair loss (1), and depression (1).

DOSAGE AND ADMINISTRATION: Treatment of initial genital herpes: One 200 mg capsule every 4 hours, while awake, for a total of 5 capsules daily for 10 days (total 50 capsules).

Chronic suppressive therapy for recurrent disease: One 200 mg capsule 3 times daily for up to 6 months. Some patients may require more drug, up to one 200 mg capsule 5 times daily for up to 6 months.

Intermittent Therapy: One 200 mg capsule every 4 hours, while awake, for a total of 5 capsules daily for 5 days (total 25 capsules). Therapy should be initiated at the earliest sign or symptom (prodrome) of recurrence.

Patients With Acute or Chronic Renal Impairment: One 200 mg capsule every 12 hours is recommended for patients with creatinine clearance ≤ 10 ml/min/1.73/m^2.

HOW SUPPLIED: Zovirax Capsules (blue, opaque) containing 200 mg acyclovir and printed with "Wellcome ZOVIRAX 200"- Bottles of 100 (NDC-0081-0991-55) and unit dose pack of 100 (NDC-0081-0991-56).

Store at 15°-30°C (59°-86°F) and protect from light.

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*In controlled studies, recurrences were totally prevented for 4 to 6 months in up to 75% of patients.

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Percutaneous Transluminal Coronary Angioplasty: Update 1985

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PERCUTANEOUS transluminal coronary angioplasty (PTCA) has become an accepted technique for the treatment of coronary artery disease. Initially, PTCA was reserved for patients with very specifically defined anatomic and clinical criteria including discrete proximal non-calcific coronary lesions involving one of the major coronary arteries in the setting of new onset stable angina pectoris.[1] Since this cautious introduction in 1977, the indications for PTCA have dramatically increased; and now encompass a wide variety of situations, including chronic stable angina, unstable angina, and acute myocardial infarction.[2-4] Furthermore, patients with unfavorable anatomy such as bifurcation stenoses, bypass graft stenosis, chronic total occlusion, multivessel disease, distal stenoses and left ventricular dysfunction are no longer excluded.[5-7]

These changing indications for PTCA may be followed by reviewing the report of our first 66 patients published in this journal in 1982, and the follow-up report summarizing an experience of 660 cases in 1984.[8-9] Our total experience updated through December 31, 1985 is summarized in *Tables 1 and 2*. The calendar year of 1985 saw a doubling of our previous number of stenoses dilated, due primarily to over 25% of the cases being multivessel PTCAs. We have now performed PTCA on more than 2,000

TABLE 1
Total PTCA Experience, 1980-1985

Year	Number Stenoses Dilated	% Primary Success
1980	10	60%
1981	60	76%
1982	179	85%
1983	381	89%
1984	599	92%
1985	1069	94%
Total:	2298	

TABLE 2
Total PTCA Experience, 1980-1985
(1985 data in parenthesis)

Site	Stenoses Dilated	% Primary Success
Anterior Descending	868 (317)	92% (94%)
Left Circumflex	563 (305)	94% (95%)
Right Coronary	685 (325)	85% (90%)
Diagonal Branch	124 (87)	96% (99%)
Vein By-Pass Graft	53 (32)	86% (88%)
Left Main Coronary	5 (3)	80% (67%)

TABLE 3
Multivessel PTCA, 1983-1985

Year	Total PTCA Cases	Multivessel PTCA Cases	Percentage
1983	341	40	12
1984	535	61	11
1985	774	221	29

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FIGURE 1-A

FIGURE 1-A: Control left coronary artery angiogram before PTCA (right anterior oblique projection).

FIGURE 1-B: "Elongated" balloon inflated in left anterior descending coronary artery.

FIGURE 1-C: Post-PTCA angiogram showing smooth opening of the long area of atherosclerotic plaque.



FIGURE 1-B



FIGURE 1-C

lesions, with a primary success rate of 93%. We wish to familiarize the reader with new developments in the technique of PTCA and to outline several exciting areas under development.

Technical Considerations

Over the Guidewire Technique: Early PTCA cases were performed with "non-steerable" balloon catheters that could be manipulated only in proximal, straight vessel segments, hence limiting patient selection severely.[1] Nearly all of our cases performed since 1982 have involved the use of "steerable" catheter systems available from ACS (Mountainview, California) and USCI (Billerica, Massachusetts). The major advantage in these systems is the ability of the operator to direct a floppy, atraumatic wire through the artery and across the stenosis before the stiffer balloon is advanced.[10] This ability to direct the balloon wire tip, could with smaller sized balloons ("low-profile"), has allowed distal branch stenoses to be approached successfully. In addition, the low profile catheter systems allow more critically obstructive coronary stenoses to be crossed without the use of significant guiding catheter support and manipulation which we feel reduces the trauma to

the coronary artery ostium.[11-13] Despite the advantages of the "over the wire" systems, we are increasingly utilizing a balloon catheter containing a non-movable but "turnable" wire, the Hartzler LPS catheter (ACS, Mountainview, California), which has allowed us to traverse extremely tight (distal or calcific) stenoses. The small shaft size also permits an approach to bifurcation lesions with sequential dilatation of both the branch and the major vessel stenosis through a single guiding catheter.[14]

New Developments

Medications: The routine peri- and post-PTCA medication regimen has changed in the past two years. Dextran is no longer used at the start of the procedure because we have witnessed several serious anaphyllactoid reactions, as have others.[15] Platelet inhibitors (aspirin and dipyridamole) are given before and after the procedure. IV heparin and nitroglycerin are also continued for 12-18 hours after PTCA. Six months of long-acting nitrates and a calcium channel blocker are prescribed. Routine placement of a pacing wire in the pulmonary artery or right ventricle is no longer performed because of several episodes of cardiac tamponade that we felt were due to small perforations magnified by the requisite use of systemic heparization during PTCA.[16]

Segmental Lesions: One of the early relative contraindications to PTCA included a coronary stenosis whose length exceeded that of the balloon.[17] This was felt to be hazardous because of the inability to shift plaque in a controlled direction, thereby allowing a smooth lumen to be created in a long segment of atheroma. The usual technique used to approach this type of lesion involves overlapping balloon inflations along the entire length of the diffuse atheroma. This may be associated with uncontrolled shifting of plaque resulting in overlapping coronary dissection lines, which increase the likelihood of abrupt closure or early restenosis. Our approach to this problem has been to develop elongated balloon catheters varying from 35 to 40 mm in length, with the expanded diameter chosen according to the size of the coronary artery to be dilated. Although our experience is small with this technique (seven cases), we feel this holds promise for the diffusely diseased vessel by allowing uniform compression of the atheroma (*Figure 1*).

Tortuous Vessel Dilatation: With growing experience, it became obvious that dilatation of a stenosis in an abruptly angulated segment carried with it increased risk of severe coronary dissection with increased probability of abrupt closure. This is especially true in a superiorly rising right coronary artery with stenosis occurring in the "shepherd's crook." We theorize that the increased complications arise from straightening the tortuous coronary segment, which would serve to widen any transverse splitting of the intima with resultant severe intimal dissection. We recently have begun using a new curved balloon catheter (ACS, Mountainview, California) that has been pre-shaped to conform to a 50 degree angle at complete balloon expansion. Fortunately, the balloon easily orients itself in the curve of the artery without the need for "torquing" and allows relatively atraumatic compression of the atheroma without distortion of the tortuous segment (*Fig. 2*). Although further work needs to be done in this area, with the development of variable angulations in balloon shape, we feel that this technique shows promise in reducing the complication and restenosis rates in patients with severely diseased tortuous segments.

Internal Mammary Graft Dilatation: The superiority in the long-term patency rate of the internal mammary graft over saphenous vein bypass grafting has now been well established.[18] With the increased use of this technique, we have encountered on several occasions stenoses occurring either at the distal anastomotic site of the internal mammary graft or in the native coronary distal to the mammary implantation. Repeat surgical intervention in these cases carries with it increased risk due to the possibility of severely traumatizing the internal mammary graft while performing the median sternotomy. We have performed PTCA in this setting successfully in nine of 10 attempts.[19] It is our feeling that this problem will become more prevalent with the increased use of the internal mammary artery for both the right and left coronary revascularization.

Multivessel Disease: Of particular interest and importance is the ever increasing absolute number (as well as percentage) of patients undergoing PTCA for multivessel disease. Our experience with multivessel PTCA through 1985 is summarized in *Table 3*. Obviously, many patients with multivessel disease, who would have previously required open heart surgery, can be treated with PTCA if their anatomy permits all anatomically significant lesions to be dilated. There may be significant problems in reference to procedure length, radiation exposure and contrast load for the patient. Experience of the angioplasty team is important in allowing these technically difficult and demanding cases to be completed rapidly and safely. It must be re-emphasized that despite the ever increasing numbers and complexity of the cases attempted (29% multivessel cases in 1985), improved equipment and operator experience have significantly enhanced the safety of the procedure. In more than 2,000 PTCAs, our primary success rate continues to be above 93%, while the acute complication rate has decreased. Our emergency surgical rate is now less than 3%, with an acute myocardial infarction rate of 1.2% and mortality rate of 0.4%.

Summary

Coronary angioplasty has gained widespread acceptance as a safe and effective technique in the treatment of



FIGURE 2-A: Control right coronary artery angiogram before PTCA. Note acute angulation of stenosed proximal segment (left anterior oblique projection with cranial angulation).

FIGURE 2-B: "Angled" balloon inflated in proximal right coronary stenosis.

FIGURE 2-C: Post-PTCA angiogram showing improvement in the stenosis without significant dissection.

FIGURE 2-A



FIGURE 2-B



FIGURE 2-C

coronary artery disease. Developments in technique have made nearly all areas of the coronary anatomy accessible to dilatation with continued high degree of success and low complication rate.

The major problem limiting PTCA at present is the high rate of re-stenosis, which exceeds 30% in the anterior descending coronary artery.[20] No medical regimen tested to date, including aspirin, dipyridamole, warfarin or nifedipine, has materially lowered this re-stenosis rate. PTCA may be easily repeated but adds to the cost and morbidity of the procedure over time.

Development of additional interventional techniques such as the actual removal of the atheroma with a cutting (arthrectomy) capsule or mechanical abrasion of the plaque may eventually have some merit in decreasing the rate of re-stenosis.[21-22] Laser technology may offer some promise for approaching totally occluded vessels and critically tight calcific stenoses if the problem of coronary perforation can be solved.[23] "Heater" probes to "tack down" areas of dissection and smooth the disrupted intima may also be useful.[24]

Solution of this enormously important problem of re-stenosis is critical for further evolution of PTCA as a

clinically useful therapeutic technique. A "breakthrough" in technology or pharmacology will be of immense significance.

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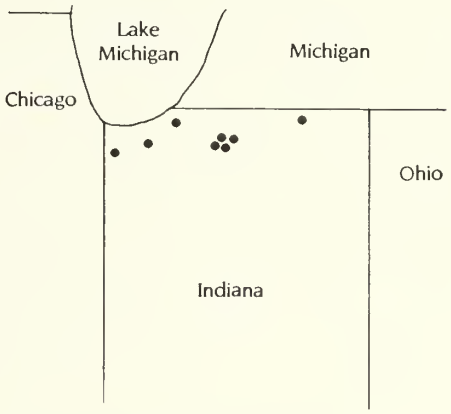
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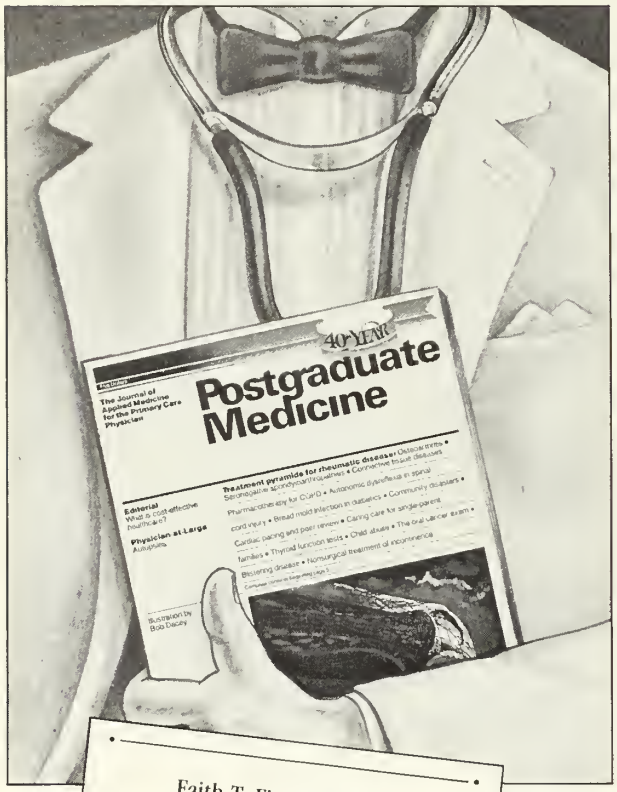
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ore prescribing, see complete prescribing information in SK&F CO. rature or *PDR*. The following is a brief summary.

VARNING

his drug is not indicated for initial therapy of edema or hyperten- ion. Edema or hypertension requires therapy titrated to the individual. this combination represents the dosage so determined, its use ay be more convenient in patient management. Treatment of hyper- ension and edema is not static, but must be reevaluated as con- itions in each patient warrant.

traindications: Concomitant use with other potassium-sparing agents h as spironolactone or amiloride. Further use in anuria, progressive al or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum assium. Hypersensitivity to either component or other sulfonamide- ved drugs.

rnings: **Do not use potassium supplements, dietary or otherwise, ss hypokalemia develops or dietary intake of potassium is markedly aired.** If supplementary potassium is needed, potassium tablets uld not be used. Hyperkalemia can occur, and has been associated n cardiac irregularities. It is more likely in the severely ill, with urine ume less than one liter/day, the elderly and diabetics with suspected onfirmed renal insufficiency. Periodically, serum K^+ levels should be ermined. If hyperkalemia develops, substitute a thiazide alone, restrict intake. **Associated widened QRS complex or arrhythmia requires mpt additional therapy.** Thiazides cross the placental barrier and ear in cord blood. Use in pregnancy requires weighing anticipated efits against possible hazards, including fetal or neonatal jaundice, mbocytopenia, other adverse reactions seen in adults. Thiazides ear and triamterene may appear in breast milk. If their use is essential, patient should stop nursing. Adequate information on use in children ot available. Sensitivity reactions may occur in patients with or with- a history of allergy or bronchial asthma. Possible exacerbation or ivation of systemic lupus erythematosus has been reported with zide diuretics.

cautions: The bioavailability of the hydrochlorothiazide component of azide' is about 50% of the bioavailability of the single entity. oretically, a patient transferred from the single entities of triamterene hydrochlorothiazide may show an increase in blood pressure or fluid ntion. Similarly, it is also possible that the lesser hydrochlorothiazide availability could lead to increased serum potassium levels. However, ensive clinical experience with 'Dyazide' suggests that these conditions e not been commonly observed in clinical practice. Angiotensin- verting enzyme (ACE) inhibitors can elevate serum potassium; use caution with 'Dyazide'. Do periodic serum electrolyte determinations ticularly important in patients vomiting excessively or receiving enteral fluids, and during concurrent use with amphotericin B or licosteroids or corticotropin [ACTH]). Periodic BUN and serum atinine determinations should be made, especially in the elderly, betics or those with suspected or confirmed renal insufficiency. mulative effects of the drug may develop in patients with impaired renal ction. Thiazides should be used with caution in patients with impaired atic function. They can precipitate coma in patients with severe liver ease. Observe regularly for possible blood dyscrasias, liver damage, er idiosyncratic reactions. Blood dyscrasias have been reported in ients receiving triamterene, and leukopenia, thrombocytopenia, anulocytosis, and aplastic and hemolytic anemia have been reported thiazides. Thiazides may cause manifestation of latent diabetes litus. The effects of oral anticoagulants may be decreased when d concurrently with hydrochlorothiazide; dosage adjustments may be essary. Clinically insignificant reductions in arterial responsiveness orepinephrine have been reported. Thiazides have also been shown to ease the paralyzing effect of nondepolarizing muscle relaxants such ubocurarine. Triamterene is a weak folic acid antagonist. Do periodic od studies in cirrhotics with splenomegaly. Antihypertensive effects be enhanced in post-sympathectomy patients. Use cautiously in pical patients. Triamterene has been found in renal stones in associa- with the other usual calculus components. Therefore, 'Dyazide' uld be used with caution in patients with histories of stone formation. w occurrences of acute renal failure have been reported in patients 'Dyazide' when treated with indomethacin. Therefore, caution is sed in administering nonsteroidal anti-inflammatory agents with zide'. The following may occur: transient elevated BUN or creatinine oth, hyperglycemia and glycosuria (diabetic insulin requirements may ltered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), reasing alkali reserve with possible metabolic acidosis. 'Dyazide' rferes with fluorescent measurement of quinidine. Hypokalemia is ommon with 'Dyazide', but should it develop, corrective measures uld be taken such as potassium supplementation or increased dietary ke of potassium-rich foods. Corrective measures should be instituted iously and serum potassium levels determined. Discontinue correc- measures and 'Dyazide' should laboratory values reveal elevated m potassium. Chloride deficit may occur as well as dilutional natremia. Concurrent use with chlorpropamide may increase the risk evere hyponatremia. Serum PBI levels may decrease without signs hyroid disturbance. Calcium excretion is decreased by thiazides. zide' should be withdrawn before conducting tests for parathyroid tion. Thiazides may add to or potentiate the action of other anti- rtensive drugs. Diuretics reduce renal clearance of lithium and ease the risk of lithium toxicity.

erse Reactions: Muscle cramps, weakness, dizziness, headache, mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other matological conditions; nausea and vomiting, diarrhea, constipation, r gastrointestinal disturbances; postural hypotension (may be avated by alcohol, barbiturates, or narcotics). Necrotizing vasculitis, sthesias, icterus, pancreatitis, xanthopsia and respiratory distress uding pneumonitis and pulmonary edema, transient blurred vision, adenitis, and vertigo have occurred with thiazides alone. Triamterene been found in renal stones in association with other usual calculus ponents. Rare incidents of acute interstitial nephritis have been rted. Impotence has been reported in a few patients on 'Dyazide', ough a causal relationship has not been established.

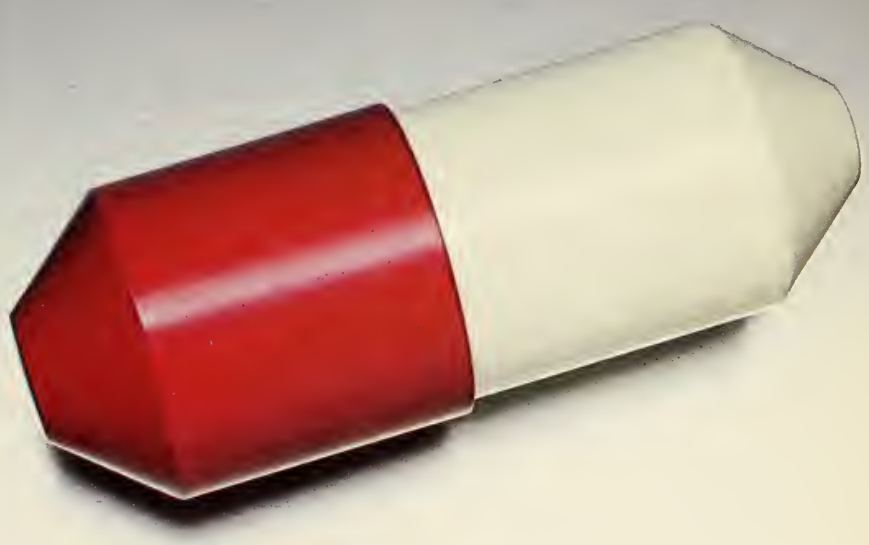
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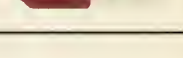
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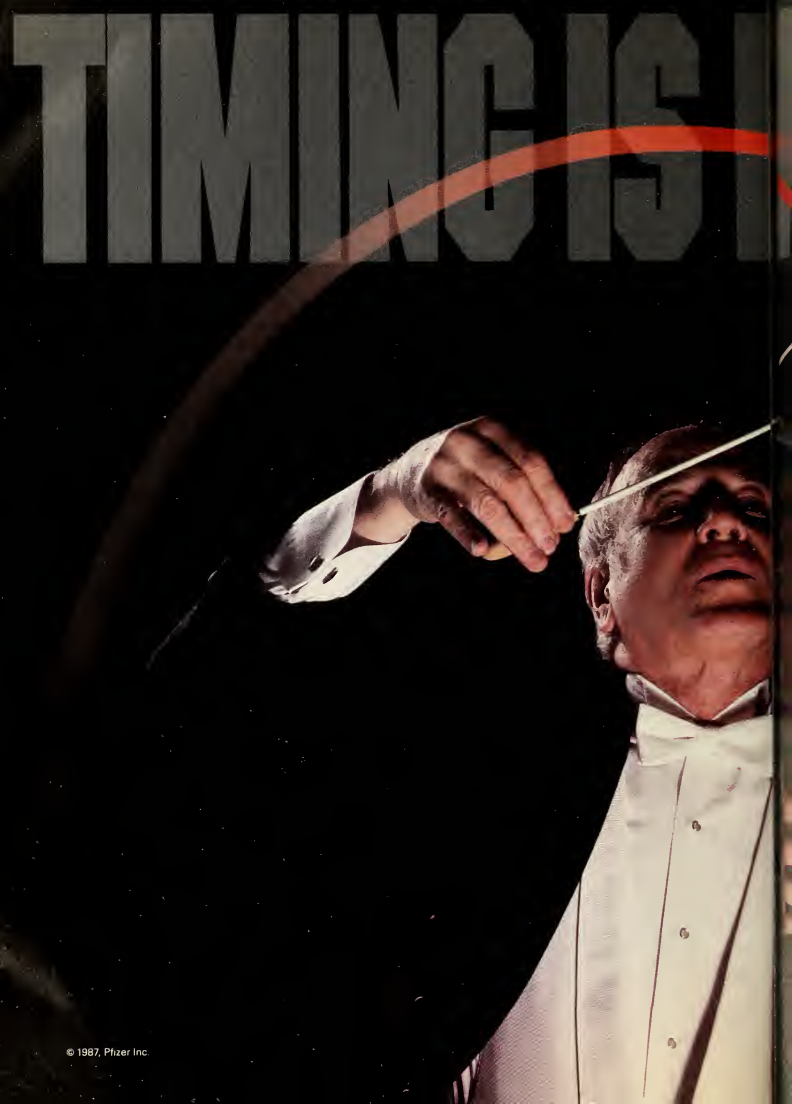


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1. Sachs R, Frank M, Fishman SK. Overview of clinical experience with glipizide. In *Glipizide. A Worldwide Review*. Princeton, NJ, Excerpta Medica, 1984, pp 163-172

GLUCOTROL® (glipizide) Tablets
Brief Summary of Prescribing Information

INDICATIONS AND USAGE: GLUCOTROL is indicated as an adjunct to diet for the control of hyperglycemia in patients with non-insulin-dependent diabetes mellitus (NIDDM, type II) after an adequate trial of dietary therapy has proved unsatisfactory.

CONTRAINDICATIONS: GLUCOTROL is contraindicated in patients with known hypersensitivity to the drug or with diabetic ketoacidosis, with or without coma, which should be treated with insulin.

SPECIAL WARNING ON INCREASED RISK OF CARDIOVASCULAR MORTALITY: The administration of oral hypoglycemic drugs has been reported to be associated with increased cardiovascular mortality as compared to treatment with diet alone or diet plus insulin. This warning is based on the study conducted by the University Group Diabetes Program (UGDP), a long-term prospective clinical trial designed to evaluate the effectiveness of glucose-lowering drugs in preventing or delaying vascular complications in patients with non-insulin-dependent diabetes. The study involved 823 patients who were randomly assigned to one of four treatment groups (*Diabetes*, 19, supp. 2:747-830, 1970).

UGDP reported that patients treated for 5 to 8 years with diet plus a fixed dose of tolbutamide (1.5 grams per day) had a rate of cardiovascular mortality approximately 2-1/2 times that of patients treated with diet alone. A significant increase in total mortality was not observed, but the use of tolbutamide was discontinued based on the increase in cardiovascular mortality, thus limiting the opportunity for the study to show an increase in overall mortality. Despite controversy regarding the interpretation of these results, the findings of the UGDP study provide an adequate basis for this warning. The patient should be informed of the potential risks and advantages of GLUCOTROL and of alternative modes of therapy.

Although only one drug in the sulfonylurea class (tolbutamide) was included in this study, it is prudent from a safety standpoint to consider that this warning may also apply to other oral hypoglycemic drugs in this class, in view of their close similarities in mode of action and chemical structure.

PRECAUTIONS: Renal and Hepatic Disease: The metabolism and excretion of GLUCOTROL may be slowed in patients with impaired renal and/or hepatic function. Hypoglycemia may be prolonged in such patients should it occur.

Hypoglycemia: All sulfonylureas are capable of producing severe hypoglycemia. Proper patient selection, dosage, and instructions are important to avoid hypoglycemia. Renal or hepatic insufficiency may increase the risk of hypoglycemic reactions. Elderly, debilitated or malnourished patients and those with adrenal or pituitary insufficiency are particularly susceptible to the hypoglycemic action of glucose-lowering drugs. Hypoglycemia may be difficult to recognize in the elderly or people taking beta-adrenergic blocking drugs. Hypoglycemia is more likely to occur when caloric intake is deficient, after severe or prolonged exercise, when alcohol is ingested, or when more than one glucose-lowering drug is used.

Loss of Control of Blood Glucose: A loss of control may occur in diabetic patients exposed to stress such as fever, trauma, infection or surgery. It may then be necessary to discontinue GLUCOTROL and administer insulin.

Laboratory Tests: Blood and urine glucose should be monitored periodically. Measurement of glycosylated hemoglobin may be useful.

Information for Patients: Patients should be informed of the potential risks and advantages of GLUCOTROL, of alternative modes of therapy, as well as the importance of adhering to dietary instructions, of a regular exercise program, and of regular testing of urine and/or blood glucose. The risks of hypoglycemia, its symptoms and treatment, and conditions that predispose to its development should be explained to patients and responsible family members. Primary and secondary failure should also be explained.

Drug Interactions: The hypoglycemic action of sulfonylureas may be potentiated by certain drugs including nonsteroidal anti-inflammatory agents and other drugs that are highly protein bound, salicylates, sulfonamides, chloramphenicol, probenecid, coumarins, monoamine oxidase inhibitors, and beta adrenergic blocking agents. *In vitro* studies indicate that GLUCOTROL binds differently than tolbutamide and does not interact with salicylate or dicumarol. However, caution must be exercised in extrapolating these findings to a clinical situation. Certain drugs tend to produce hyperglycemia and may lead to loss of control, including the thiazides and other diuretics, corticosteroids, phenothiazines, thyroid products, estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetics, calcium channel blocking drugs, and isoniazid. A potential interaction between oral miconazole and oral hypoglycemic agents leading to severe hypoglycemia has been reported. Whether this interaction also occurs with the intravenous, topical, or vaginal preparations of miconazole is not known.

Carcinogenesis, Mutagenesis, Impairment of Fertility: A 20-month study in rats and an 18-month study in mice at doses up to 75 times the maximum human dose revealed no evidence of drug-related carcinogenicity. Bacterial and *in vivo* mutagenicity tests were uniformly negative. Studies in rats of both sexes at doses up to 75 times the human dose showed no effects on fertility.

Pregnancy: Pregnancy Category C. GLUCOTROL (glipizide) was found to be mildly tetotoxic in rat reproductive studies at all dose levels (5-50 mg/kg). This tetotoxicity has been similarly noted with other sulfonylureas, such as tolbutamide and tolazamide. The effect is perinatal and believed to be directly related to the pharmacologic (hypoglycemic) action of GLUCOTROL. In studies in rats and rabbits no teratogenic effects were found. There are no adequate and well controlled studies in pregnant women. GLUCOTROL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Because recent information suggests that abnormal blood glucose levels during pregnancy are associated with a higher incidence of congenital abnormalities, many experts recommend that insulin be used during pregnancy to maintain blood glucose levels as close to normal as possible.

Nonteratogenic Effects: Prolonged severe hypoglycemia has been reported in neonates born to mothers who were receiving a sulfonylurea drug at the time of delivery. This has been reported more frequently with the use of agents with prolonged half-lives. GLUCOTROL should be discontinued at least one month before the expected delivery date.

Nursing Mothers: Since some sulfonylurea drugs are known to be excreted in human milk, insulin therapy should be considered if nursing is to be continued.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS: In controlled studies, the frequency of serious adverse reactions reported was very low. Of 702 patients, 11.8% reported adverse reactions and in only 1.5% was GLUCOTROL discontinued.

Hypoglycemia: See PRECAUTIONS and OVERDOSAGE sections.

Gastrointestinal: Gastrointestinal disturbances, the most common, were reported with the following approximate incidence: nausea and diarrhea, one in 70; constipation and gastralgia, one in 100. They appear to be dose-related and may disappear on division or reduction of dosage. Chloestatic jaundice may occur rarely with sulfonylureas. GLUCOTROL should be discontinued if this occurs.

Dermatologic: Allergic skin reactions including erythema, morbilliform or maculopapular eruptions, urticaria, pruritus, and eczema have been reported in about one in 70 patients. These may be transient and may disappear despite continued use of GLUCOTROL; if skin reactions persist, the drug should be discontinued. Porphyria cutanea tarda and photosensitivity reactions have been reported with sulfonylureas.

Hematologic: Leukopenia, agranulocytosis, thrombocytopenia, hemolytic anemia, aplastic anemia, and pancytopenia have been reported with sulfonylureas.

Metabolic: Hepatic porphyria and disulfiram-like alcohol reactions have been reported with sulfonylureas. Clinical experience to date has shown that GLUCOTROL has an extremely low incidence of disulfiram-like reactions.

Endocrine Reactions: Cases of hyponatremia and the syndrome of inappropriate antidiuretic hormone (SIADH) secretion have been reported with this and other sulfonylureas.

Miscellaneous: Dizziness, drowsiness, and headache have been reported in about one in fifty patients treated with GLUCOTROL. They are usually transient and seldom require discontinuance of therapy.

OVERDOSAGE: Overdosage of sulfonylureas including GLUCOTROL can produce hypoglycemia. If hypoglycemic coma is diagnosed or suspected, the patient should be given a rapid intravenous injection of concentrated (50%) glucose solution. This should be followed by a continuous infusion of a more dilute (10%) glucose solution at a rate that will maintain the blood glucose at a level above 100 mg/dL. Patients should be closely monitored for a minimum of 24 to 48 hours since hypoglycemia may recur after apparent clinical recovery. Clearance of GLUCOTROL from plasma would be prolonged in persons with liver disease. Because of the extensive protein binding of GLUCOTROL (glipizide), dialysis is unlikely to be of benefit.

DOSAGE AND ADMINISTRATION: There is no fixed dosage regimen for the management of diabetes mellitus with GLUCOTROL, in general, it should be given approximately 30 minutes before a meal to achieve the greatest reduction in postprandial hyperglycemia.

Initial Dose: The recommended starting dose is 5 mg before breakfast. Geriatric patients or those with liver disease may be started on 2.5 mg. Dosage adjustments should ordinarily be in increments of 2.5-5 mg, as determined by blood glucose response. At least several days should elapse between titration steps.

Maximum Dose: The maximum recommended total daily dose is 40 mg.

Maintenance: Some patients may be effectively controlled on a once-a-day regimen, while others show better response with divided dosing. Total daily doses above 15 mg should ordinarily be divided.

HOW SUPPLIED: GLUCOTROL is available as white, dye-free, scored diamond-shaped tablets imprinted as follows: 5 mg tablet—Pfizer 411 (NDC 5 mg 0049-4110-66) Bottles of 100, 10 mg tablet—Pfizer 412 (NDC 10 mg 0049-4120-65) Bottles of 100.

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Hemoglobin E in Indiana

TED BLOCH, M.D.
TJIEN O. OEI, M.D.
Indianapolis

Abstract

Hemoglobin E is one of the most prevalent hemoglobin (Hb) variants in the world, and is seen almost exclusively in the Southeast Asian population. The hematologic manifestations of Hb E alone or with an associated thalassemia are relatively unfamiliar to Indiana physicians. Hb E trait (Hb AE) and homozygous hemoglobin E (Hb EE) are benign conditions; however, coexistence of Hb E and thalassemia may result in severe anemia. A Laotian family is presented with individuals affected by Hb AE and Hb EE. In view of the influx of persons from Southeast Asia, these hematologic disorders are worthy of increased awareness.

HEMOGLOBIN E (Hb E), a common hemoglobin variant in Southeast Asia, has recently been found quite often in North America, because of the Indochinese resettlement program in the United States and the Save the Boat people program in Canada. The incidence of Hb E in Southeast Asia ranges from 3% in Vietnam[1] to 35% in Laos.[2] In the last few years, approximately 5,000 Southeast Asian refugees have emigrated to Indiana. In view of the influx of persons with Hb E, this hemoglobinopathy and its interaction with other hematologic disorders are worthy of increased awareness. In this report, we describe a family with Hb E trait (Hb AE) and homozygous Hb E (Hb EE). The spectrum of Hb E conditions is emphasized.

Report of Three Cases

A recently emigrated 24-year-old Laotian woman (patient M) presented at a local county health facility for prenatal care. She complained of some lethargy, but was otherwise in good health. There was no history of malaria. Physical examination was unremarkable.

Pertinent laboratory results are listed in the *Table*. Iron studies were normal.

The peripheral smear disclosed numerous target erythrocytes and severe microcytosis. Slight polychromatophilia and poikilocytosis were also present (*Figure 1*).

Hemoglobin electrophoresis at pH 8.6 (cellulose acetate) showed a prominent slow-moving band at the C site (*Figure 2*). Electrophoresis at pH 6.2 (citrate agar) now revealed a slow-moving band at the A site (*Figure 3*). The abnormal band prompted evaluation of the husband (patient F) and only child (patient S). Both were asymptomatic. There was no history of malaria. Pertinent laboratory results, including electrophoretic studies, are listed in the *Table*.

Materials and Methods

The hematologic data were determined on a Coulter IV (Coulter Electronics). Electrophoretic studies were performed on citrate agar and cellulose acetate using standard laboratory techniques.

The isopropanol solubility test (I.S.T.) was performed on freshly

TABLE

TEST	NORMALS	PATIENT M	PATIENT F	PATIENT S
Hemoglobin (gm/dl)	M: 16 ± 2			
	F: 14 ± 2	11.1	14.7	11.3
Hct. (%)	M: 47 ± 5			
	F: 42 ± 5	34	46	36
RBC (10^{12}/1)	M: 5.4 ± 0.7			
	F: 4.8 ± 0.6	5.31	5.27	4.72
MCV (f1)	M: 87 ± 7			
	F: 90 ± 9	63.7	87	76
WBC (10^9/1)	7.8 ± 3	8.7	8.8	7.9
RDW (%)	13 ± 1.5	14.3	14.8	15
Hb E (%)	0	98	34	33
Hb A* (%)	96-99	0	66	67
Hb F (%)	<0.5	2	0	0
I.S.T. -	–	+	+	+

*Hemoglobin A_2 comigrates with Hb E and Hb C on cellulose acetate.

From the Dept. of Pathology, Indiana University School of Medicine, Indianapolis.

Correspondence and reprints: Tjien O. Oei, M.D., Indiana University Hospital, N440, 926 W. Michigan St., Indianapolis, Ind. 46223.

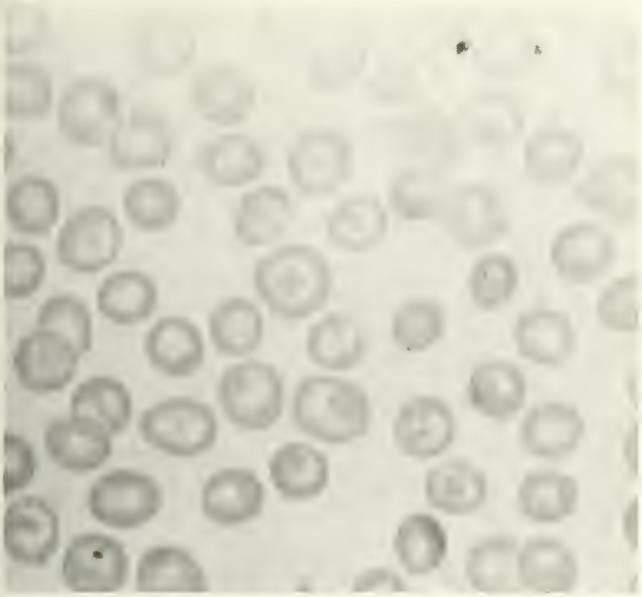


FIGURE 1: Peripheral blood smear with numerous target erythrocytes. (Patient M, Wright's stain, 630X).



FIGURE 2: Cellulose acetate electrophoresis at pH 8.6 showing the slow-moving band at the C site. The upper bands represent normal controls. (Patient M).



FIGURE 3: Citrate agar electrophoresis at pH 6.2 showing the band now in the A position, diagnostic for Hb E. The upper bands represent normal controls. (Patient M).

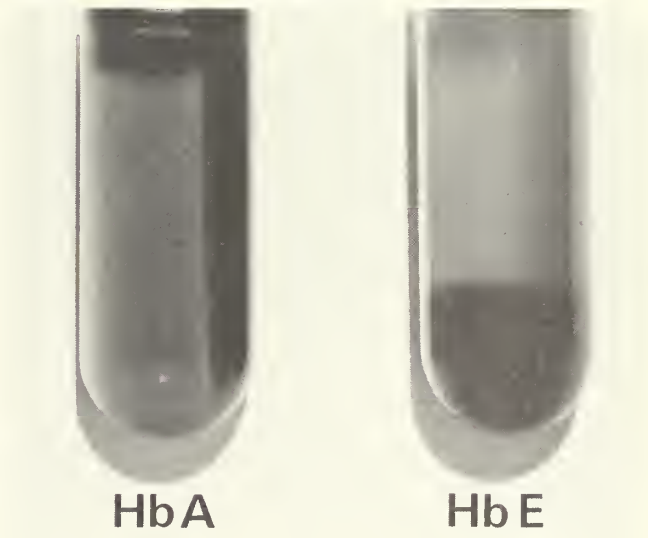


FIGURE 4: Comparison samples of Patient M and HbAA treated with isopropanol. Note the (reddish-brown) flocculent precipitate at the base of the Hb E tube, indicating a positive test after 20 minutes of incubation.

prepared hemolysate. Isopropanol (17%) in 0.1 M tris-HC1 buffer (2 ml, pH 7.4) was added to the hemolysate (0.2 ul) and incubated at 37°C. Positive samples yielded cloudiness at 5-10 minutes and copius reddish-brown flocculent precipitate at 15-20 minutes (*Figure 4*).

Discussion

Patient M has a slow-moving hemoglobin, which is approximately 98% of the total hemoglobin, that represents

Hb EE. Patient F and patient S have Hb AE. Hb E is one of the most prevalent hemoglobin variants in the world, ranking third behind Hb S and Hb C. It is almost exclusively seen in Southeastern Asians.

With the advent of the "Save the Boat People" program in Canada and the Indochinese resettlement program in the United States, thousands of Southeastern Asians migrated to North America. With them came a variety of hemoglobin abnormalities, many of which are unfamiliar to most U.S. physicians. These include Hb AE, Hb EE, Hb E and beta-thalassemia (Hb E-β thal) and Hb E and alpha-thalassemia (Hb E-α thal). Awareness of the clinical and laboratory characteristics of these disorders is important to avoid the misdiagnosis of existing thalassemia syndromes which may result in inappropriate iron supplementation for microcytosis.

The Hb E molecule is produced when a single base pair substitution results in replacement of the glutamic acid residue by lysine at position 26 of the beta chain. This abnormality was first described by Itano *et al.* in a patient of Guatemalan origin[3] and simultaneously by Chernoff *et al.*[4] in 1954. The first cases of Hb AE[5] and Hb EE[6] in the United States were described by Fairbanks *et al.* in 1979 and 1980, respectively.

Hb AE trait is an asymptomatic state where slight to moderate microcytosis (MCV; 65-80 fl) and erythrocytosis (M-5.34, F-4.99 x 10^{12}/1) develop. Electrophoretic studies reveal 30-35% Hb E. These patients are usually found during pedigree studies of more severe syndromes or through screening programs.

Hb EE is also usually asymptomatic. It is characterized by absent or mild anemia, marked microcytosis (MCV; 55-70 Fl), and erythrocytosis (M-5.50, F-5.25 x 10^{12}/1). The blood smear shows predominantly microcytes and target cells, which may account for up to 50% of the cell population present. Electrophoretic studies show 97%-99% Hb E and the remainder Hb F. This state is easily differentiated from the trait by the large number of target cells.

When a patient with Hb E-β thal presents, the clinical picture is of a severe hemolytic anemia which mimics Cooley's anemia (homozygous beta-thalassemia). The clinical severity is variable and is determined primarily by the type of interacting thalassemia. Cases with Beta° thalassemia (absent Beta chain production) are more severe than Beta+ thalassemia (decreased Beta chain production). Severely affected patients exhibit severe anemia (hemoglobin 2-6 mg/dl), gross hepatosplenomegaly, poor physical growth and hemolytic skeletal changes. At the other end of the spectrum, they will have moderate anemia and splenomegaly. The majority of those affected have an intermediate clinical course. Blood smears show severe hypochromic, microcytic anemia with marked anisopoikilocytosis characterized by numerous tear drop and target forms. Basophilic stippling and nucleated red cells may also be present.

Hb E-β thal is by far the most common symptomatic thalassemia in Southeast Asia. It is surprising that a simple mutation of the beta chain would interact with Beta-thalassemia to produce such a severe hematologic disorder. The severity of disease is due to inefficient Hb E chain synthesis. The mechanism for decreased hemoglobin E beta chain production is the result of decreased production or increased instability of the beta chain $_{m}$RNA. Traeger *et al.* showed that there is defective production of beta chain in homozygous and heterozygous Hb E patients. However, the beta chains that were produced were stable. They found that there is reduced amounts of Hb E $_{m}$RNA in incubated reticulocytes.[7] Further studies show a decrease in Hb E $_{m}$RNA from erythroblast nuclei to erythroblast cytoplasm when bone marrow aspirates from Hb EE patients were analyzed supporting the unstable $_{m}$RNA hypothesis.[8]

Another important hematologic disease commonly found in Southeast Asia is alpha-thalassemia. It is therefore not surprising that cases of Hb E-α thal occur. This family of diseases has a range of clinical presentation which depends on the number of absent alpha chains genes that are inherited. Much of the original work on alpha-thalassemia and its interaction with Hb E was published by Tuchinda.[9,10]

The most severe of the Alpha thalassemia group is Hb E- Hb H disease (alpha-thalassemia$_1$/alpha-thalassemia$_2$, Hb E). The mild alpha thalassemia determinant indicates loss of one alpha chain gene and is designated alpha-thalassemia $_2$ while the severe determinant, alpha-thalassemia $_1$, indicates loss of both alpha chain genes from the chromosome. Hb E-Hb H disease represents 3 absent alpha chains genes and one beta chain mutation. They present with moderate to severe anemia, jaundice, hepatosplenomegaly, growth retardation and hemolytic skeletal abnormalities. Blood smears show a marked hypochromic, microcytic anemia with marked anisopoikilocytosis and numerous target erythrocytes (15%-35%). Polychromasia, basophilic stippling and nucleated red cells are present. Incubation with brilliant cresyl blue produces rare red cell inclusions of hemoglobin H. Similar treatment of pure hemoglobin H disease (alpha-thal$_1$/alpha-thal$_2$) results in numerous inclusions which helps to differentiate the two states. Electrophoretic studies reveal a reduced Hb E level (13%-20%), Hb A (70%-80%), Hb F (3%-5%) and Hb Barts (6%-10%). Occasionally, a faint band of Hb H is seen. The reason for the decreased or absent Hb H is the reduction of beta chain synthesis. The usual surplus of beta chains to produce the A_4 tetramers (Hb H) are not present because of the Hb E gene. The E_4 tetramers will migrate with hemoglobin A.

Patients with two absent alpha chain genes (alpha-thal$_1$Hb E or alpha-thal$_2$/

alpha thal$_2$ Hb E) are usually asymptomatic. Blood smears reveal a mild hypochromic microcytic anemia, erythrocytosis, and mild anisopoikilocytosis with 10% target erythrocytes. Electrophoretic studies reveal 20%-25% Hb E and Hb A.

Hb E can also be associated with one absent alpha chain gene. The patients are also asymptomatic. Blood smears show a very mild hypochromic microcytic anemia with erythrocytosis, slight anisopoikilocytosis and approximately 5% target erythrocytes. Electrophoretic studies show 25%-30% Hb E. This type of patient is easily missed, with the slightly decreased concentration of Hb E serving as the guide to the diagnosis.

Iron deficiency anemia is commonly seen in Southeast Asian immigrants secondary to poor nutrition and a host of intestinal parasites. Lack of adequate iron results in decreased globin synthesis. A phenotype of Hb E- α thal $_2$ results in patients with Hb E trait and iron deficiency. Wasi *et al.* reported a 13%-25% Hb E range in this population.[11] Treatment with iron supplements restored the Hb E concentration. Iron studies are therefore essential when evaluating a patient with presumed Hb E- α thal.

One of the most useful, inexpensive and easily performed tests to confirm the presence of hemoglobin E is the I.S.T. All three patients were positive when tested. The I.S.T. is also positive with unstable hemoglobins such as Hb H and Hb Genova.[12] The test is useful when separation of co-migrating forms such as Hb O arab or Hb C is necessary.

Unlike most hemoglobinopathies, which are associated with a marked increase in maternal mortality, prematurity and neonatal mortality, pregnant patients with Hb AE and Hb EE have a relatively benign course. Ong reported his experience with 28 pregnant patients with Hb E (20 Hb AE, 8 Hb EE) and found no difference in live birth rates, prematurity rates, maternal deaths or fetal abnormalities when compared to normal controls.[13] In contradistinction, pregnant patients with Hb E- β thal are not as fortunate. Case reports by Ferguson *et al.*[14] and Lie-Injo *et al.*[15] reveal recurrent, early neonatal death, prematurity and fetal growth retardation. A large series of these patients is not available because of the low frequency of this condition in adults, secondary to early death of affected children.

Hb E can be seen in association with numerous clinical syndromes. Patients with Hb AE and Hb EE have moderate microcytosis but are clinically asymptomatic. Individuals with Hb E-β thal show marked hematologic abnormalities with a moderate to severe clinical course. The genotype of the patient dictates the hematologic variants and the clinical course in patients with Hb E- α thal. Iron studies, electrophoretic studies and the I.S.T. are useful when evaluating these patients.

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Medicine's Lighter Moments

TED L. GRISELL, M.D.
Indianapolis



THE FAT APPENDIX

IT WASN'T INDICATED that there was anything unusual about the request when Dr. John M. Young, a urologist at Methodist Hospital in Indianapolis, asked me to see a patient for a possible acute abdomen. The story over the phone was that a woman had been admitted a couple of hours earlier with signs and symptoms suggestive of some acute abdominal emergency, and with findings in the urinary tract suggesting the possibility of urinary tract disease.

I walked into the examining room and found that she was not in a hospital bed because a hospital bed probably would have collapsed, or at least been totally inadequate for her size. The woman was on exhibit at the State Fair and was advertised as the fattest woman in the world. The accuracy of that advertising may have been subject to debate, but there was no question that she weighed about 700 pounds.

Examination revealed she had typical nausea, vomiting and right lower quadrant pain, elevated white count, and negative urinary tract infection. The presumptive diagnosis was acute appendicitis. She was taken to the operating room on two gurneys, the fancy name for hospital carts. These carts were lashed together to provide space for a person of this size.

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In the operating room, an attempt was made to prepare the patient's abdomen in the usual manner. However, the extreme thickness of the abdominal wall and the layers of fat provided a moving target for the attempts at scrubbing the abdomen. The belly wall and layers of fat moving up and down like angry ocean waves provided a very unsatisfactory, unstable abdominal wall for either the preparation or the impending surgery.

After some cerebration, a decision was made to get some large strips of adhesive tape and, by taping the abdominal wall over the patient's left side and down to the floor, the right side of the abdomen was stabilized, at least to a degree. The right side of the abdomen was then locally prepped, appropriate drapes were applied, the patient's anesthetic was begun and the operation proceeded.

Surprisingly, an abdominal wall that was at least two feet thick was reduced by taping the layers of fat to the floor on the left side of the operating table. The thickness of the wall was thereby reduced to an estimated 12 inches. We were able, with some good help, to expose the appendix, found it to be gangrenous, removed it routinely, closed the abdomen, and departed for a postoperative libation, one of the very few I indulged myself in during my years of surgery.

The sequel to this story was that the patient recovered, and left the hospital in five or six days, afebrile, with the wound healing satisfactorily. She was advised to report to our office for final examination in about three weeks.

Three weeks later, the woman appeared in the office. She was a little disheartened because she felt she might be losing her position as the fattest woman in the world since she had lost 24 pounds during her recovery period.

We were reluctant to allow her on our examining table because it was not designed for that size patient. Instead, we suggested she stand in front of the desk and raise her skirt so we could examine the incision and see if it was healing properly. When she did so, lo and behold, there was no incision visible.

As we stood there looking rather astonished, she finally said, "Oh, you want to see my scar." Then she raised her skirt in the rear, and the incision could be seen—just above the right buttox. This was, of course, due to the fact that the skin layers had been stretched to the left lateral position at the time of her operation and had now resumed their normal anatomical position.

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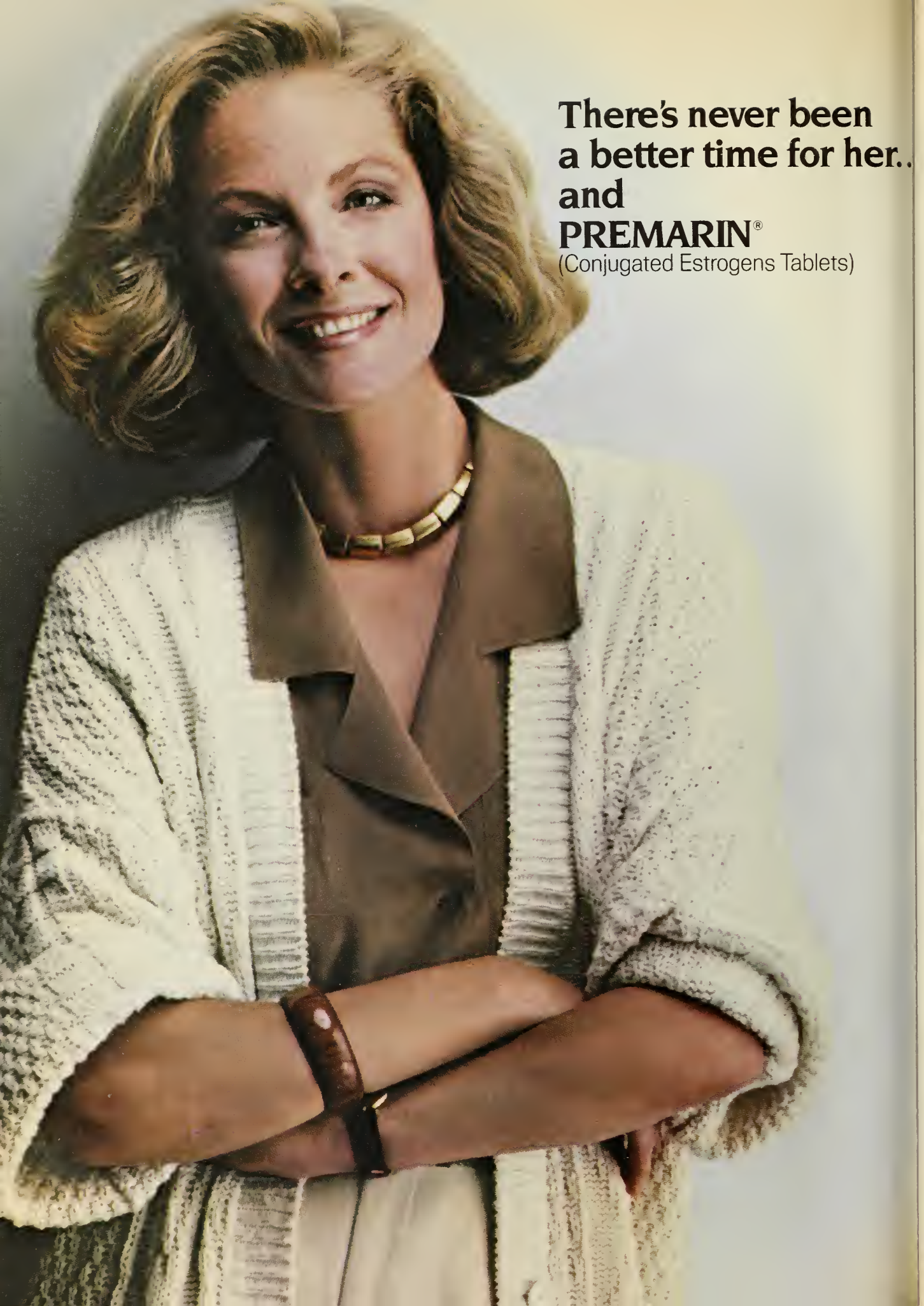
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Significantly reduced risk of endometrial hyperplasia

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PREMARIN used alone does not adversely affect lipid levels. In fact, a clinical study has shown a significant increase in HDL cholesterol—from 49.7 mg/dL to 56.4 mg/dL—and decrease in LDL cholesterol—from 165.1 mg/dL to 138.1 mg/dL—after one year of therapy with PREMARIN, 0.625 mg.[5]

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*PREMARIN is indicated for moderate-to-severe vasomotor symptoms.

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For moderate-to-severe vasomotor symptoms

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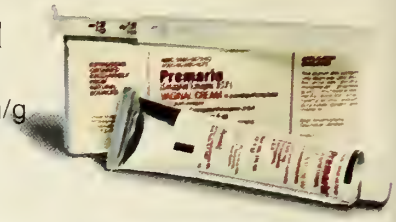
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For atrophic vaginitis

PREMARIN®
(Conjugated Estrogens)

Vaginal Cream

0.625mg/g



BRIEF SUMMARY *(FOR FULL PRESCRIBING INFORMATION AND PATIENT INFORMATION, SEE PACKAGE CIRCULARS.)*

PREMARIN® Brand of conjugated estrogens tablets, USP
PREMARIN® Brand of conjugated estrogens Vaginal Cream in a nonliquefying base

1. ESTROGENS HAVE BEEN REPORTED TD INCREASE THE RISK DF ENDOMETRIAL CARCINOMA.

Three independent case control studies have reported an increased risk of endometrial cancer in postmenopausal women exposed to exogenous estrogens tor more than one year. This risk was independent of the other known risk factors for endometrial cancer. These studies are further supported by the finding that incidence rates ot endometrial cancer have increased sharply since 1969 in eight different areas of the United States with population-based cancer reporting systems, an increase which may be related to the rapidly expanding use of estrogens during the last decade. The three case control studies reported that the risk of endometrial cancer in estrogen users was about 4.5 to 13.9 times greater than in nonusers. The risk appears to depend on both duration of treatment and on estrogen dose. In view of these findings, when estrogens are used tor the treatment of menopausal symptoms, the lowest dose that will control symptoms should be utilized and medication should be discontinued as soon as possible. When prolonged treatment is medically indicated, the patient should be reassessed on at least a semiannual basis to determine the need for continued therapy. Although the evidence must be considered preliminary, one study suggests that cyclic administration ot low doses of estrogen may carry less risk than continuous administration; it theretore appears prudent to utilize such a regimen. Close clinical surveillance ot all women taking estrogens is important. In all cases of undiagnosed persistent or recurring abnormal vaginal bleeding, adequate diagnostic measures should be undertaken to rule out malignancy. There is no evidence at present that "natural" estrogens are more or less hazardous than "synthetic" estrogens at equiestrogenic doses.

2. ESTROGENS SHOULD NDT BE USED DURING PREGNANCY.

The use of female sex hormones, both estrogens and progestogens, during early pregnancy may seriously damage the offspring. It has been shown that females exposed in utero to diethylstilbestrol, a non-steroidal estrogen, have an increased risk of developing in later life a form of vaginal or cervical cancer that is ordinarily extremely rare. This risk has been estimated as not greater than 4 per 1,000 exposures. Furthermore, a high percentage ot such exposed women (from 30% to 90%) have been tound to have vaginal adenosis, epithelial changes of the vagina and cervix. Although these changes are histologically benign, it is not known whether they are precursors of malignancy. Although similar data are not available with the use of other estrogens, it cannot be presumed they would not induce similar changes. Several reports suggest an association between intrauterine exposure to temale sex hormones and congenital anomalies, including congenital heart detects and limb reduction detects. One case control study estimated a 4.7-told increased risk ot limb reduction detects in infants exposed in utero to sex hormones (oral contraceptives, hormone withdrawal tests tor pregnancy, or attempted treatment tor threatened abortion). Some of these exposures were very short and involved only a few days of treatment. The data suggest that the risk of limb reduction detects in exposed tetuses is somewhat less than 1 per 1,000. In the past, temale sex hormones have been used during pregnancy in an attempt to treat threatened or habitual abortion. There is considerable evidence that estrogens are ineffective for these indications, and there is no evidence trom well controlled studies that progestogens are effective for these uses. If PREMARIN is used during pregnancy, or if the patient becomes pregnant while taking this drug, she should be apprised ot the potential risks to the tetus, and the advisability of pregnancy continuation.

DESCRIPTIDN: PREMARIN (conjugated estrogens, USP) contains a mixture of estrogens, obtained exclusively trom natural sources, blended to represent the average composition of material derived from pregnant mares' urine. It contains estrone, equilin, and 17α-dihydroequilin, together with smaller amounts of 17α-estradiol, equilenin, and 17α-dihydroequilenin as salts of their sulfate esters. Tablets are available in 0.3 mg, 0 625 mg, 0 9 mg, 1.25 mg, and 2.5 mg strengths ot conjugated estrogens. Cream is available as 0 625 mg conjugated estrogens per gram.

INDICATIONS AND USAGE: PREMARIN (conjugated estrogens tablets, USP): Moderate-to-severe *vasomotor* symptoms associated with the menopause. (There is no evidence that estrogens are effective tor nervous symptoms or depression without associated vasomotor symptoms and they should not be used to treat such conditions.) **Osteoporosis (abnormally low bone mass).** Atrophic vaginitis. Kraurosis vulvae. Female castration.

PREMARIN (conjugated estrogens) Vaginal Cream is indicated in the treatment ot atrophic vaginitis and kraurosis vulvae. PREMARIN HAS NDT BEEN SHOWN TO BE EFFECTIVE FOR ANY PURPOSE DURING PREGNANCY AND ITS USE MAY CAUSE SEVERE HARM TD THE FETUS (SEE BOXED WARNING).

Concomitant Progestin Use: The lowest effective dose appropriate tor the specitic indication should be utilized. Studies of the addition of a progestin for 7 or more days ot a cycle of estrogen administration have reported a lowered incidence ot endometrial hyperplasia. Morphological and biochemical studies of the endometrium suggest that 10 to 13 days of progestin are needed to provide maximal maturation of the endometrium and to eliminate any hyperplastic changes. Whether this will provide protection trom endometrial carcinoma has not been clearly established. There are possible additional risks which may be associated with the inclusion of progestin in estrogen replacement regimens. (See PRECAUTIONS.) The choice ot progestin and dosage may be important; product labeling should be reviewed to minimize possible adverse effects.

CONTRAINDICATIONS: Estrogens should not be used in women (or men) with any of the following conditions: 1. Known or suspected cancer of the breast except in appropriately selected patients being treated tor metastatic disease. 2. Known or suspected estrogen-dependent neoplasia. 3. Known or suspected pregnancy (See Boxed Warning). 4. Undiagnosed abnormal genital bleeding. 5. Active thrombophlebitis or thromboembolic disorders. 6. A past history ot thrombophlebitis, thrombosis, or thromboembolic disorders associated with previous estrogen use (except when used in treatment ot breast or prostatic malignancy).

WARNINGS: Long-term continuous administration ot natural and synthetic estrogens in certain animal species increases the frequency ot carcinomas ot the breast, cervix, vagina, and liver. There are now reports that estrogens increase the risk ot carcinoma of the endometrium in humans. (See Boxed Warning.) At the present time there is no satisfactory evidence that estrogens given to postmenopausal women increase the risk of cancer ot the breast, although a recent study has raised this possibility. There is a need for caution in prescribing estrogens for women with a strong family history ot breast cancer or who have breast nodules, tibrocystic disease, or abnormal mammograms. A recent study has reported a 2- to 3-fold increase in the risk ot surgically confirmed gallbladder disease in women receiving postmenopausal estrogens.

Adverse effects ot oral contraceptives may be expected at the larger doses of estrogen used to treat prostatic or breast cancer or postpartum breast engorgement; it has been shown that there is an increased risk ot thrombosis in men receiving estrogens for prostatic cancer and women tor postpartum breast engorgement. Users ot oral contraceptives have an increased risk ot diseases, such as thrombophlebitis, pulmonary embolism, stroke, and myocardial infarction. Cases ot retinal thrombosis, mesenteric thrombosis, and optic neuritis have been reported in oral contraceptive users. An increased risk of postsurgery thromboembolic complications has also been reported in users of oral contraceptives. If teasible, estrogen should be discontinued at least 4 weeks betore surgery ot the type associated with an increased risk of thromboembolism, or during periods ot prolonged immobilization. Estrogens should not be used in persons with active thrombophlebitis, thromboembolic disorders, or in persons with a history ot such disorders in association with estrogen use. They should be used with caution in patients with cerebral vascular or coronary artery disease. Large doses (5 mg conjugated estroge per day), comparable to those used to treat cancer of the prostate and breast, have been shown to increase t risk of nontatal myocardial infarction, pulmonary embolism and thrombophlebitis. When doses of this size a used, any of the thromboembolic and thrombotic adverse effects should be considered a clear risk.

Benign hepatic adenomas should be considered in estrogen users having abdominal pain and tendernes abdominal mass, or hypovolemic shock. Hepatocellular carcinoma has been reported in women taking estroge containing oral contraceptives. Increased blood pressure may occur with use ot estrogens in the menopause a blood pressure should be monitored with estrogen use. A worsening ot glucose tolerance has been observed patients on estrogen-containing oral contraceptives. For this reason, diabetic patients should be caretu observed. Estrogens may lead to severe hypercalcemia in patients with breast cancer and bone metastases.

PRECAUTIONS: Physical examination and a complete medical and family history should be taken prior to t initiation of any estrogen therapy with special reference to blood pressure, breasts, abdomen, and pelvic organ and should include a Papanicolaou smear. As a general rule, estrogen should not be prescribed tor longer th one year without another physical examination being performed. Conditions intluenced by tluid retention such asthma, epilepsy, migraine, and cardiac or renal dysfunction, require careful observation. Certain patients m develop manifestations of excessive estrogenic stimulation, such as abnormal or excessive uterine bleedin mastodynia, etc. Prolonged administration ot unopposed estrogen therapy has been reported to increase the ri ot endometrial hyperplasia in some patients. Oral contraceptives appear to be associated with an increas incidence ot mental depression. Patients with a history of depression should be caretully observed. Preexisti uterine leiomyomata may increase in size during estrogen use. The pathologist should be advised ot estrog therapy when relevant specimens are submitted. If jaundice develops in any patient receiving estrogen, t medication should be discontinued while the cause is investigated. Estrogens should be used with care in patier with impaired liver function, renal insufficiency, metabolic bone diseases associated with hypercalcemia, or young patients in whom bone growth is not complete. If concomitant progestin therapy is used, potential ris may include adverse effects on carbohydrate and lipid metabolism.

The following changes may be expected with larger doses of estrogen:

a. Increased sulfobromophthalein retention.

b. Increased prothrombin and tactors VII, VIII, IX, and X; decreased antithrombin 3; increased nc epinephrine-induced platelet aggregability.

c. Increased thyroid binding globulin (TBG) leading to increased circulating total thyroid hormone, measured by PBI, T4 by column, or T4 by radioimmunoassay. Free T3 resin uptake is decreased, reflecting t elevated TBG; free T4 concentration is unaltered.

d. Impaired glucose tolerance.

e. Decreased pregnanediol excretion.

t. Reduced response to metyrapone test.

g. Reduced serum tolate concentration.

h. Increased serum triglyceride and phospholipid concentration. As a general principle, the administration any drug to nursing mothers should be done only when clearly necessary since many drugs are excreted in hum milk.

ADVERSE REACTIDNS: The tollowing have been reported with estrogenic therapy, including oral contraceptive breakthrough bleeding, spotting, change in menstrual tlow; dysmenorrhea; premenstrual-like syndrom amenorrhea during and after treatment; increase in size of uterine libromyomata; vaginal candidiasis, change cervical erosion and in degree ot cervical secretion; cystitis-like syndrome; tenderness, enlargement, secretic (ot breasts); nausea, vomiting, abdominal cramps, bloating; cholestatic jaundice; chloasma or melasma whi may persist when drug is discontinued; erythema multitorme; erythema nodosum; hemorrhagic eruption; loss scalp hair; hirsutism; steepening ot corneal curvature, intolerance to contact lenses; headache, migrain dizziness, mental depression, chorea; increase or decrease in weight; reduced carbohydrate tolerance; aggrav tion ot porphyria; edema; changes in libido.

ACUTE DVERDDSAGE: May cause nausea, and withdrawal bleeding may occur in temales.

DOSAGE AND ADMINISTRATION:

PREMARIN® Brand of conjugated estrogens tablets, USP

1. *Given cyclically for short-term use only.* For treatment ot moderate to severe *vasomotor* symptoms, atroph vaginitis, or kraurosis vulvae associated with the menopause (0.3 to 1.25 mg or more daily). The lowest dose th will control symptoms should be chosen and medication should be discontinued as promptly as possibl Administration should be cyclic (eg, three weeks on and one week off). Attempts to discontinue or tap medication should be made at three- to six-month intervals.

2. *Given cyclically:* Female castration. Osteoporosis. Female castration—1.25 mg daily, cyclically. Adju upward or downward according to response ot the patient. For maintenance, adjust dosage to lowest level th will provide effective control. Osteoporosis—0.625 mg daily. Administration should be cyclic (eg, three weel on and one week off).

Patients with an intact uterus should be monitored for signs ot endometrial cancer and appropriate measure taken to rule out malignancy in the event ot persistent or recurring abnormal vaginal bleeding.

PREMARIN® Brand of conjugated estrogens Vaginal Cream

Given cyclically for short-term use only. For treatment ot atrophic vaginitis or kraurosis vulvae.

The lowest dose that will control symptoms should be chosen and medication should be discontinued a promptly as possible.

Administration should be cyclic (eg, three weeks on and one week off).

Attempts to discontinue or taper medication should be made at three-to-six month intervals.

Usual dosage range: 2 to 4 g daily, intravaginally, depending on the severity ot the condition.

Treated patients with an intact uterus should be monitored closely for signs of endometrial cancer an appropriate diagnostic measures should be taken to rule out malignancy in the event ot persistent or recurrin abnormal vaginal bleeding.

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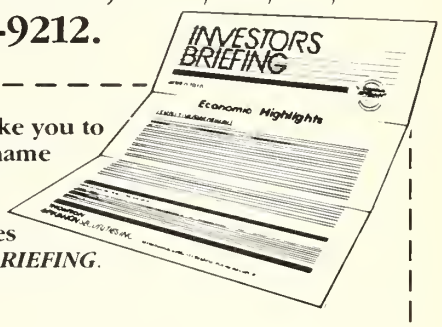
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BRITISH GERIATRICS, 1986

JEFFREY C. DARNELL, M.D.
Indianapolis

I RECENTLY RETURNED from Manchester, England after working for two months with an academic department of geriatric medicine. Their efforts are very impressive, particularly when compared to our more modest geriatric endeavors in the United States. This is an especially interesting scenario because of the seeming paradox, at least in geriatrics, of the British spending less and receiving more. There are probably several factors underlying this apparent paradox, and the British experience may be useful to us.

'ATTRIBUTES OF BRITISH HEALTH CARE OUTWEIGH DEFICIENCIES, AND THE SYSTEM FUNCTIONS WELL'

Geriatric medicine in Britain has evolved under several unique influences, not the least of which was the initiation of the National Health Service in 1948.[1] This was primarily a political decision and was based on general concepts of social justice. From the beginning the primary aim of the National Health Service was, and remains, the development and delivery of comprehensive health care services for all citizens. The enormity of this program at the outset was compounded by the mandated haste of transition. Furthermore, the impetus for change was and is significantly politically based, e.g., the demands of constituents were and are persuasive. Therefore, at its inception, the structure of the National Health Service represented the best estimates of the various planners, constrained by some socio-economic realities. Subsequent changes have often been responses to perceived needs as judged by both providers and recipients.

At its beginning, the National Health Service inherited large hospitals for the poor and chronically ill. These workhouses cared for large numbers of institutionalized individuals and they became, from the beginning, the responsibility of the pioneering geriatricians. The interest of these geriatricians, some confronted with literally hundreds of institutionalized patients, was immediately and necessarily directed toward rehabilitation. The prospect of large scale discharges from these recently acquired facilities was also appealing to the National Health Service. The birth of the National Health Service, with its admirable goal of quality health care for all, the acquisition of large workhouses and the economy of discharges through large scale rehabilitation efforts, essentially set the course for geriatric departments to follow. This unique set of circumstances is, in no small part, responsible for the success and high quality of British geriatrics today.

British geriatricians have, from the beginning, embraced the responsibility for providing services for elderly living in their districts and at the same time they have intensified and tailored their rehabilitation services. In a similar fashion the British psychogeriatricians inherited large mental institutions, many of which had been underserved medical backwaters. They, too, were immediately and necessarily engaged in assessment, treatment and discharge as appropriate of their clientele. The evolution of this process has produced the developed psychogeriatric units of today with their active assessment wards, day hospitals, long-stay wards, and extensive domiciliary visitations.

Cost has been a limiting, although not necessarily guiding factor. Change has been initiated, in part, as the result of perceived needs, and assessment of cost effectiveness has not always been required prior to general implementation of services. Nevertheless, a quality health care system has been developed at a cost considerably less than that of most other Western nations. In 1982, Britain spent 5.9% of its gross national product on health and this was the lowest rate among 11 countries including the U.S. (10.6%).[2]

The proliferation of medical-surgical procedures has been controlled in Britain partly by restricting the number of practitioners trained to perform the various procedures. The human cost of this comparative shortage of established services is unknown, but this shortage undoubtedly contributes to the reduced overall economic cost. In many cases, ample and generous space was

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available for all services from the beginning. This tended to minimize the requirement for capital investment and doubtless influenced the development of services. The plans of the pioneers took flight unconstrained by space limitations and, over the years, these visions have substantially materialized.

The evolution of British health care services has taken place in an atmosphere requiring primarily the definition of problem areas. Great pride was and is taken in the compassion and generosity of the society as a whole. If segments of the society were and are wanting for services, and particularly health care services, then services should be developed to meet these needs. The impetus for their implementation is primarily the concern of society and is not generally dependent upon documentation of the cost effectiveness or efficacy of the proposed service.

On geriatric services, both medical and psychiatric, enormous efforts are invested in maintaining patients in the community. This almost always represents the best interest of the patients and at the same time minimizes cost. It is argued that savings accrued through the large scale prevention of permanent institutionalization can finance considerable ambulatory and short-term care, including rehabilitation. Therefore, the argument goes, failure to invest in prevention and rehabilitation is false economy, reducing the quality of life and increasing costs in the long run.

The economy of the British health care system is, nevertheless, not immediately apparent. Virtually every district has a hospital, often large and generously staffed. However, these facilities are commonly old, and expensive refurbishment has not been regularly undertaken. In addition, substantial space has been devoted to day care and rehabilitation and is thus staffed only during weekdays. Various special services, especially surgical, are comparatively scarce and are not undertaken with the frequency observed in other developed countries. The proliferation of technology has been checked to a certain extent, and sophisticated equipment such as CT scanners, MRI, etc., is not available in every hospital or district. Wages in the health care service tend also to be lower than other European and Western countries. This combination of decreased capital expenditures, restricted specialty services, constrained technology and equipment and relatively low wages likely accounts for a significant proportion of the British health care savings. In addition, the extraordinary efforts to reduce hospitalizations, particularly among the elderly, are undoubtedly successful to some extent.

Maintaining the infirm and disabled in the community is eased by a substantial support network. Remuneration of the disadvantaged is universal, and basic needs such as food and housing are subsidized for the needy. Old people's housing is particularly useful in that considerable disability can be tolerated and supported in council housing at a cost far less than nursing home care. Sheltered housing employs only a property warden, but this individual is expected to aid and assist the tenants. Other domiciliary services can be mustered, including district nurses and nonprofessional home helpers, to maintain a moderately disabled individual. In Part 3 accommodations, essentially all services are provided but by non-professional staff. Again, other providers attend the residents and every effort is made to maintain them in this environment until death. The net result is a reduction in the number of patients requiring expensive hospital-like, long-term care. Those patients who are admitted to the hospital are generally conventionally evaluated and managed. In fact, their stays in hospital tend to be relatively protracted, in part because of a diminished investigatory pace. In addition, the overriding desire to discharge patients to home rather than institutional care is a prolonging influence.

'The Elderly Fare Particularly Well; Their Care Is Not Likely Surpassed in Other Societies'

I believe some of the important attributes of the British health care system are:

1) The universality of health care coverage.

2) The comparatively low overall cost of care.

3) The highly developed preventive and rehabilitative care services including day hospitals, respite care, Part 3 accommodations and innumerable domiciliary care services.

4) The integration of providers into functioning multidisciplinary teams.

5) The interest of the general electorate in health care services and their willingness to subsidize care for the disadvantaged.

6) A quality academic system attracting first class students to the medical professions and insuring the adequacy of their training.

Important problems facing the system would seem to include, among others:

1) Queuing for indicated procedures, both therapeutic and investigative.

2) Widespread, aging and deteriorating physical facilities.

3) Shortages of established services such as dialysis and transplantation.

4) A relatively underpaid service corps, including doctors, nurses, therapists, and essentially the spectrum of workers.

On balance, the attributes of British health care far outweigh the deficiencies and the system generally functions admirably well. The elderly fare particularly well, and their care is not likely surpassed in many other societies. The wealth of resources available to British geriatricians has been carefully nurtured but is, in part, a product of another era. In particular, the physical space devoted to geriatrics could not be duplicated in today's cost-conscious environment. The inevitable decline of aging facilities may eventually result in diminishing British resources.

The past almost four decades have witnessed the renaissance of geriatric medicine. The future is uncertain and, although the British system probably is not exportable on a similar scale to other societies, the course has been admirably set.

I thank Professor J. C. Brocklehurst for his hospitality in receiving me at the University of Manchester and for permitting me to follow his Department of Geriatric Medicine. He and his geriatric colleagues have had notable success in carrying out the roles of service, teaching, and research, and I hope the lessons of their long experience can be helpful to us.

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FUTURE FILE

CONTINUED FROM PAGE 317

ACS Cancer Conference

The Second National Conference on Cancer Prevention and Detection will be conducted by the American Cancer Society on June 25 to 27 at the Westin Hotel in Seattle, Washington.

For full information write the Society at 90 Park Avenue, New York, N.Y. 10016.

Berkshire Conference

The Third Annual Berkshire Medical Conference will be conducted in July at the Country Inn and Conference Center at Jiminy Peak, Hancock, Mass., in the heart of the Berkshires. It is sponsored by the Berkshire Medical Center, University of Massachusetts Medical School.

The conference will consist of two courses: "Advances in Cardiology," July 16-18, and "Common Emergencies in General Medicine," July 23-25. Each course is accredited for 16 Category 1 hours. The fee is $295 for one course, or $500 for both.

Contact the Berkshire AHEC, 725 North St., Pittsfield, Mass. 01201—(413) 499-4161, ext. 2417.

Menopause Symposium

The Scott and White Clinic announces two CME meetings. "Menopause: Consequences and Treatment Strategies" is the subject of a National Symposium to be conducted at South Padre Island Hilton Resort, Texas, June 17 to 20. The same meeting site will be used for the "Seventh Annual Internal Medicine Review."

For information, contact: Office of CME, Scott and White, Temple, Texas 76508—(817) 774-4073.

Physician in Management

Seminar I and Seminar II on "The Physician in Management" is scheduled for June 22-26 at the Antlers Hotel, Colorado Springs, Colo. Each seminar is worth 31 CME credit hours.

The correspondent is Sherry Mason, American Academy of Medical Directors, 4830 W. Kennedy Blvd., Suite 648, Tampa, Fla. 33609—(813) 873-2000.

Clinical Home Care

"The Second Conference on Clinical Home Care in the 1980s: Economics, Implementation and Ethical Issues" will be conducted June 25-26 at the Wisconsin Center, Madison. It is accredited for 13 Category 1 hours.

The correspondent is Sarah Aslakson, 465B WARF Bldg., 610 Walnut St., Madison, Wisc. 53705.

Child Advocacy

"Child Advocacy as a New Role for Professionals" is the title of a conference to be conducted Sept. 10-12 at the Concourse Hotel, Madison, Wisc.

The course will be oriented to physicians, lawyers, health professionals and educators. It is accredited for 15 Category 1 hours. The fee for physicians is $250. The conference will address advocacy issues such as child abuse and neglect, joint custody, teenage pregnancy, and termination of parents' rights.

The correspondent is Ann Bailey, WARF Bldg., Room 456, 610 Walnut St., Madison, Wisc. 53705.

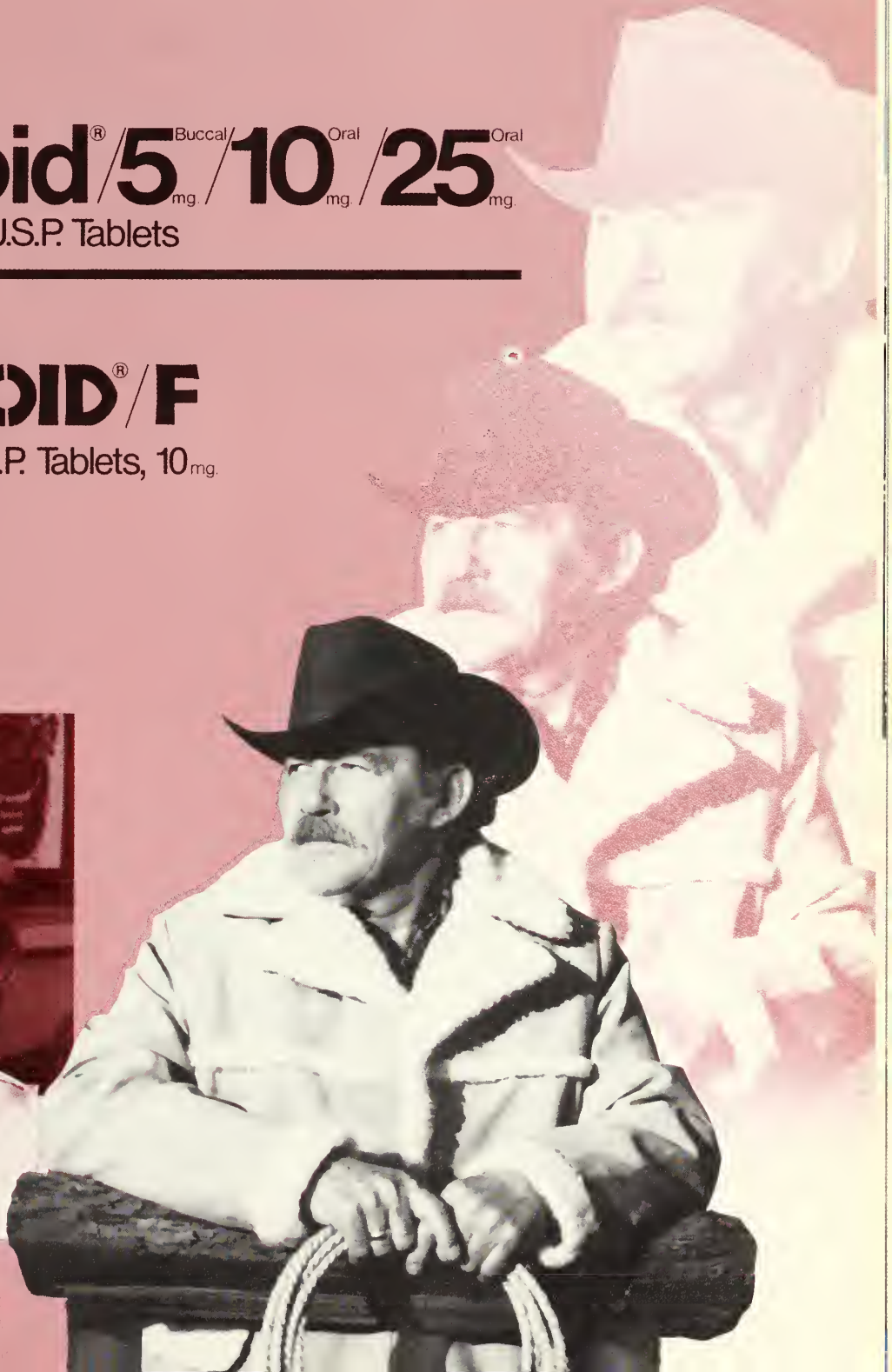
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Changing Economics in Medical Practice

MASON R. GOODMAN, M.D.
Indianapolis

TODAY'S MEDICAL practices are, of necessity, dynamic rather than static entities. Even long-established and historically successful practices are undergoing radical change in response to the many economic pressures that seem to be reshaping modern medicine. These changes encompass both the "art" and "science" of medicine; and even the most conservative prognoses predict their continuation for the forseeable future.

The economic forces at work in today's medical community are making (and will continue to make) physicians scrutinize new programs, practices and services to achieve and then maintain the quality of care our patients deserve and demand. Our patients, their employers, and their insurers have of late become more sophisticated consumers of our medical "product." It is therefore incumbent upon us to examine our practice styles and our philosophies of "doing business" as medical professionals. The initials "P.C." offer more than tax benefits and protection from individual financial liability. In today's stringent economic climate, they offer us a challenge to review the proficiency with which we operate as small businesses in an extremely competitive marketplace.

Dr. Goodman, a pulmonary diseases specialist, is Medical Director of the new Walther Medical Research Institute in Indianapolis.

Correspondence: 3266 N. Meridian St., Indianapolis, Ind. 46208.

For years physicians have tended to segregate the "business of medicine" from the "practice of medicine." We have tended to delegate the tasks related to the practical function of our practices to our accountants and office managers. There is, however, far more than a superficial correlation between the principles of sound business administration and those of successful practice management. The physician who truly succeeds in the era of "third-party medicine" will be the physician who can adapt his philosophies of practice management to the principles of sound business administration and development.

'A More Businesslike Approach to Practice Management Is Required of the Physician Who Truly Wishes to Achieve or Maintain Practice Security over the Next Few Years'

While medical practices may vary widely in their scope and the range of patient services they offer, each has two things in common with the others. Each is a business, and each of these businesses has only two commodities to offer "for sale": the physician's time and expertise. Since expertise is open to degrees of highly subjective interpretation, this article will limit itself to a consideration of time as our sole commodity in the medical marketplace. We are reimbursed for our time by multiple sources; but this commodity is increasingly being paid for by large employers and health care providers, each of which seeks to impose restrictions on the cost of our services. This article reviews the economics of a medical practice and relates the various elements of health care delivery to the concept of cost centers vs. profit centers in a business environment.

In most cases, the professional component of a medical practice generates the bulk of its gross revenue. Today there are three prevailing modalities for delivery of professional services: traditional fee-for-service, capitated third-party provider systems, and salaried positions in various health care programs. Regardless of the professional modality, a direct relationship can be established between time spent seeing patients and compensation. In the past, physicians who wished to increase income could do so by working longer hours. In recent years, however, the supply/demand curve for physicians has shifted so dramatically that it is no longer possible to even stabilize income (let alone increase income) by this direct method. Today, this problem is further magnified by the increasing cost of doing business . . . total professional and practice overhead . . . in an increasingly constrictive medical environment.

If our professional time is the major "profit center" in our practices, and if the traditional relationship of time to income no longer holds true, what other factors must we consider to get a true picture of the "ethnomics" of

medicine today? Clearly, any function in a practice that reduces quality of care in the interest of increased revenue is not within the scope of this review. Rather, those elements of sound business practice that heighten professionalism, improve patient compliance and generate patient satisfaction are those worthy of mention.

Any analysis of the "business of medical practice" should focus on ways to maximize practice operating efficiency and increase patients' overall satisfaction with their dealings with our practices. There are three key concepts to consider in this area:

1) Increasing patients' satisfaction by making them aware of your practice's respect for their time;

2) Making better use of the "non-direct patient care time" available in one's practice to improve operating efficiency and increase patient services; and

3) Analyzing the physical and procedural variables that can have a positive impact on operating efficiency and patient satisfaction.

RESPECT FOR YOUR PATIENTS' TIME can be communicated in a number of overt and subtle ways. Since this sort of respect is visible evidence of the physician's recognition of the patient's importance, these "low cost" changes can produce a lot of instant gratification on both parties' part. Every effort should be made to schedule effectively, and special care should be taken with the patient who is new to your practice. One might have a staff member come out to the waiting area to greet the new patient and take a few moments to explain the practice and its procedures as an alternative to passing a "new patient form" on a clipboard out through the check-in window. Special attention should be paid to seeing patients as promptly as possible, and explaining delays courteously when they inevitably do occur. Open clinics work well when understood by the patient, especially if the clinic is held during "convenience hours." Finally, conserving the patient's time by offering a spectrum of expanded patient services is usually perceived very positively by patients in a wide variety of practice situations.

NON-DIRECT PATIENT CARE TIME—that time spent delivering services in support of the treatment process—has not been effectively developed as a practice "profit center" by many physicians. However, when expanded patient services serve to enhance practice professionalism they can be effectively used to increase practice profitability as well.

'The Physician Who Truly Succeeds in the Era of Third-Party Medicine Will Be the Physician Who Can Adapt His Philosophies of Practice Management to the Principles of Sound Business Administration and Development.'

Examples abound in a variety of professional settings. Orthopedic appliances are often available for purchase from physicians' offices. Laboratory testing (when volume and quality control make it practical) and certain types of radiologic services are being offered in more and more practices. Routine electrocardiography is being performed more frequently by primary care physicians as an alternative to having all tracings interpreted on consultation. Ultrasound, laser procedures and other technologies are becoming more cost-effective and are thus more readily available for in-office application. Ophthalmologists for years have provided ocular prostheses, eyeglasses and contact lenses. Many other disciplines, such as rheumatology and certain subspecialties of surgery and internal medicine, have employed occupational, physical, speech, hearing, dietary and other types of registered therapists, nurses and psychologists to extend their professional contact with the patient and offer a broader and more convenient practice style.

In the past few years, physicians have been increasingly and effectively employing the dispensing of pharmaceuticals from their offices in states where this is a time-honored tradition. The application of pharmaceutical industry technology to a formerly cumbersome procedure has made available the ability to deliver appropriately prepackaged medication to the physician's office. These "patient ready" preparations are then available for dispensing in dosage increments the physician commonly prescribes. This precludes the physician's investment in a large pharmaceutical inventory. The cost, labor and potential for error involved in in-office repackaging of pharmaceuticals is eliminated. It minimizes the space required for a dispensary and allows the physician to present an elegant product to his patients, thus enhancing the physician's professional appearance. Computerized labeling, and simplified record-keeping and in-office promotional aids are offered as well by at least one company that provides unit-of-use pharmaceuticals in Indiana and nationally.

The decreasing number of independent pharmacists and the lack of strong physician-pharmacist relationships has increased the viability of this patient-convenient practice enhancement opportunity. Our patients want convenience, and they have a much higher comfort level when receiving prescrip-

tion medications from their personal physician. This confidence seems to apply equally to the other previously mentioned patient services when they are provided within the context of the medical practice. Still other forms of expanded patient services include weight control and smoking cessation programs, which may allow for positive practice positioning in today's competitive medical community.

These somewhat entrepreneurial activities have in common the practitioner's desire to offer maximum convenience for the patient while enhancing ancillary profit centers where appropriate. Prescription dispensing in particular allows the physician to capture practice income that was formerly inaccessible. The end results of such increased physician or physician-office contact with the patient are: enhanced rapport, improved accounts receivable and better practice marketing.

PHYSICAL AND PROCEDURAL VARIABLES should also be analyzed if one wishes to reap the full measure of benefit available from the types of practice enhancement already discussed. A critical assessment of the need for space, office rent, types and number of employees, billing procedures and potential computerization of the office can identify areas of needed improvement. Developing a professional approach to dealing with third-party payors and increasing one's awareness of cash-flow position will help minimize overhead and improve the practice's "bottom line."

In summary, a more businesslike approach to practice management is required of the physician who truly wishes to achieve or maintain practice security over the next few years. Taking advantage of an increasing number of patient-convenient practice enhancement opportunities will enable the physician to continue to maintain the critical role of patient's advocate and gatekeeper to quality health care.

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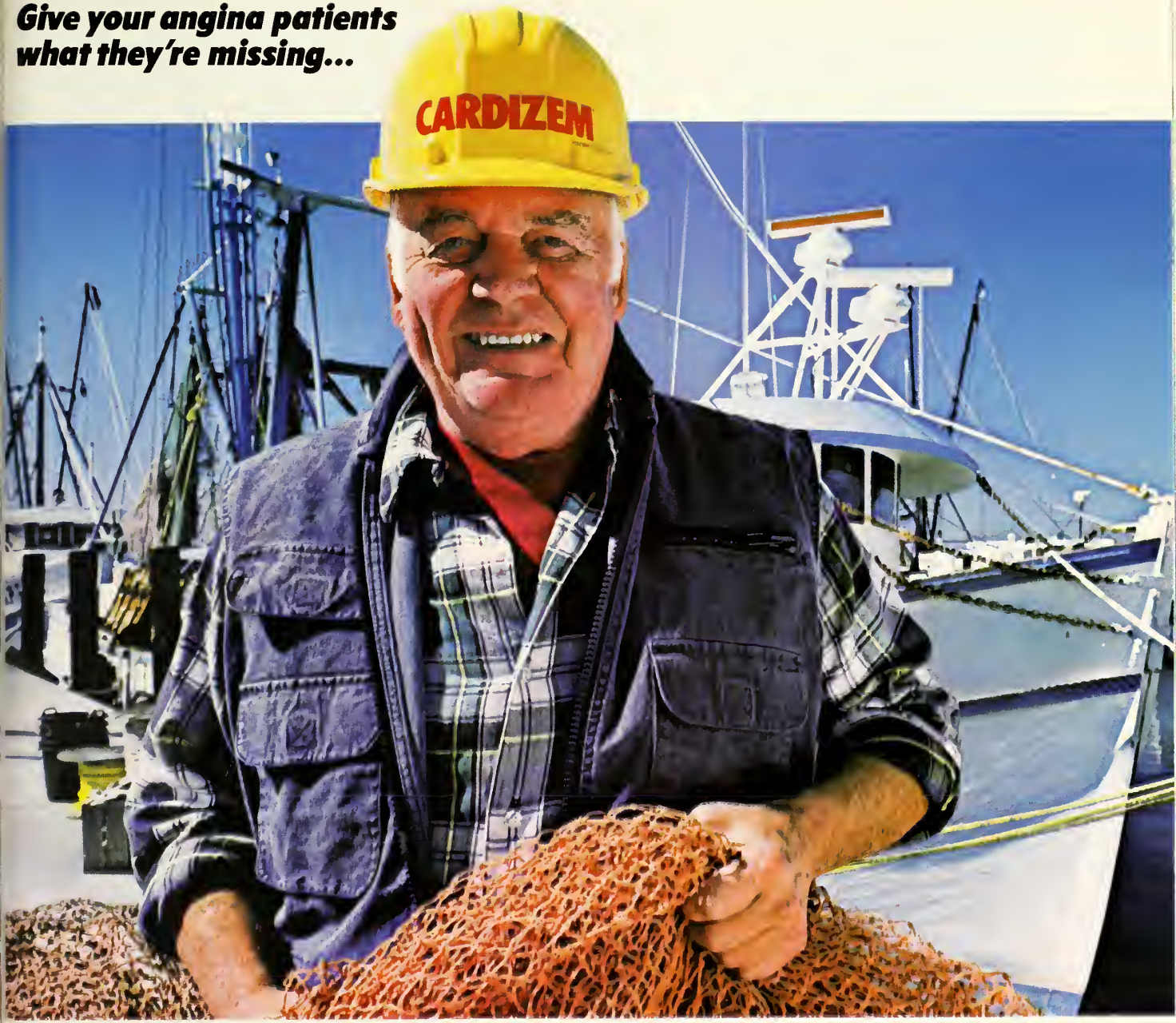
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CONTRAINDICATIONS
CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, and (3) patients with hypotension (less than 90 mm Hg systolic).

WARNINGS

1. ***Cardiac Conduction.*** *CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (six of 1,243 patients for 0.48%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of diltiazem.*
2. ***Congestive Heart Failure.*** *Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt).*
   Experience with the use of CARDIZEM alone or in combination with beta-blockers in patients with impaired ventricular function is very limited. Caution should be exercised when using the drug in such patients.
3. ***Hypotension.*** *Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.*
4. ***Acute Hepatic Injury.*** *In rare instances, significant elevations in enzymes such as alkaline phosphatase, CPK, LDH, SGOT, SGPT, and other symptoms consistent with acute hepatic injury have been noted. These reactions have been reversible upon discontinuation of drug therapy. The relationship to CARDIZEM is uncertain in most cases, but probable in some. (See PRECAUTIONS.)*

PRECAUTIONS
General. *CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any new drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histalogical changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes, however, these changes were reversible with continued dosing.*

Drug Interaction. *Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS.)*

Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers or digitalis is usually well tolerated. Available data are not sufficient, however, to predict the effects of concomitant treatment, particularly in patients with left ventricular dysfunction or cardiac conduction abnormalities. In healthy volunteers, diltiazem has been shown to increase serum digoxin levels up to 20%.

Carcinogenesis, Mutagenesis, Impairment of Fertility. *A 24-month study in rats and a 21-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response in in vitro bacterial tests. No intrinsic effect on fertility was observed in rats.*

Pregnancy. *Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/pasthatal studies, there was some reduction in early individual pup weights and survival rates. There was an increased incidence of stillbirths at doses of 20 times the human dose or greater.*

There are no well-controlled studies in pregnant women; therefore, use CARDIZEM in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. *Diltiazem is excreted in human milk. One report suggests that concentrations in breast milk may approximate serum levels. If use of CARDIZEM is deemed essential, an alternative method of infant feeding should be instituted.*

Pediatric Use. *Safety and effectiveness in children have not been established.*

ADVERSE REACTIONS
Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded.

In domestic placebo-controlled trials, the incidence of adverse reactions reported during CARDIZEM therapy was not greater than that reported during placebo therapy.

The following represent occurrences observed in clinical studies which can be at least reasonably associated with the pharmacology of calcium influx inhibition. In many cases, the relationship to CARDIZEM has not been established. The most common occurrences as well as their frequency of presentation are: edema (2.4%), headache (2.1%), nausea (1.9%), dizziness (1.5%), rash (1.3%), asthenia (1.2%). In addition, the following events were reported infrequently (less than 1%):

Cardiovascular:	*Angina, arrhythmia, AV block (first degree), AV block (second or third degree — see conduction warning), bradycardia, congestive heart failure, flushing, hypotension, palpitations, syncope*
Nervous System:	*Amnesia, gait abnormality, hallucinations, insomnia, nervousness, paresthesia, personality change, somnolence, tinnitus, tremor*
Gastrointestinal:	*Anorexia, constipation, diarrhea, dysgeusia, dyspepsia, mild elevations of alkaline phosphatase, SGOT, SGPT, and LDH (see hepatic warnings), vomiting, weight increase*
Dermatologic:	*Petechiae, pruritus, photosensitivity, urticaria*
Other:	*Amblyopia, dyspnea, epistaxis, eye irritation, hyperglycemia, nasal congestion, nocturia, osteoarticular pain, polyuria, sexual difficulties*

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: alopecia, gingival hyperplasia, erythema multiforme, and leukopenia. However, a definitive cause and effect between these events and CARDIZEM therapy is yet to be established. *Issued 7/86*

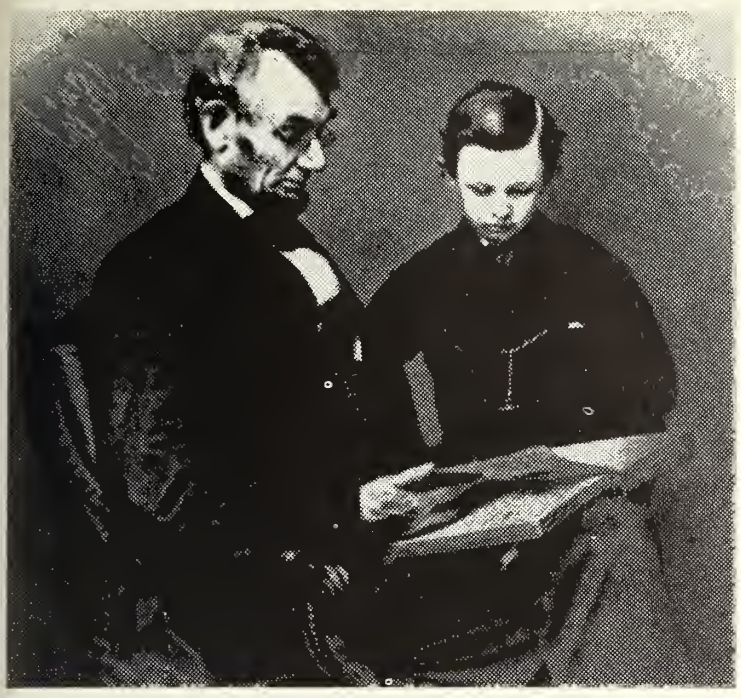
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What Every Physician Should Know About the Medical Licensing Board

RONALD L. DYER, J.D.
Indianapolis

THE MEDICAL Licensing Board of Indiana consists of seven members appointed by the Governor with terms of four years each. While state law does not preclude a member from serving more than two consecutive terms, current practice has been that members typically serve no longer than two terms in succession. By statute, the seven members consist of five M.D.s, one D.O., and one consumer member. Currently, those members are:

John D. Miller, M.D., Bluffton, Ind.
Martin J. O'Neill, M.D., Valparaiso, Ind.
George H. Rawls, M.D., Indianapolis, Ind.
Gilbert M. Wilhelmus, M.D., Evansville, Ind.
Deanna S. Porte, M.D., Hammond, Ind.
John Hinton, D.O., West College Corner, Ind.
Ronald E. Elberger, J.D., Indianapolis, Ind.

Normally, the Medical Licensing Board meets one full day per month, generally the last Thursday of each month, throughout the year.

Compensation

Members of the Medical Licensing Board receive $50 per day for attending meetings plus reimbursement for expenses incurred in attending meetings.

The author is Associate Director and General Counsel, Indiana State Medical Association, Indianapolis.

Disciplinary Powers

The Board has the power to impose various sanctions against a practitioner if it finds any of the following has occurred:

1. The practitioner has perpetrated a fraud or a material deception in order to obtain a medical license.
2. The practitioner has engaged in fraud or material deception in the course of professional services or activities.
3. The practitioner has advertised services in a false or misleading manner.
4. The practitioner has been convicted of a crime that has a direct bearing on his ability to practice medicine competently.
5. The practitioner has knowingly violated any rule promulgated by the Board.
6. The practitioner has continued to practice although he has become unfit due to: professional incompetence; failure to keep abreast of current professional theory or practice; physical or mental disability; addiction or severe dependency on alcohol or other drugs that endanger the public by impairing the practitioner's ability to practice safely.
7. The practitioner has engaged in a course of lewd or immoral conduct in connection with delivery of services.
8. The practitioner has knowingly prescribed, sold, or administered any drug classified as a narcotic, addicting, or dangerous drug to an addict.
9. The practitioner has had disciplinary action taken against him in another state.

The Board has the power to order a practitioner to submit to reasonable physical or mental examinations if the practitioner's physical or mental capacity to practice safely has been called into question as a result of disciplinary proceedings.

In addition, the Board may impose any of the following sanctions if it finds the practitioner has committed any of the offenses mentioned above:

1. Permanently revoke the practitioner's license.
2. Suspend the practitioner's license.
3. Censure the practitioner.
4. Issue a letter of reprimand.
5. Place the practitioner on probation and require the physician to report regularly.
6. Limit the practitioner's practice to areas prescribed by the Board.
7. Require the practitioner to continue or renew professional education.

Summary Suspension

The Board also has the power to issue the summary suspension of a physician's license for up to 90 days in advance of a hearing if the Board is presented with evidence that convinces it that the practitioner *represents a clear and immediate danger to the public* health and safety if the practitioner is allowed to continue practice.

The power of the Medical Licensing Board to issue summary suspensions without giving the physician an opportunity to present evidence has been a source of much concern over the last several years. While the Board continues to have the statutory power to issue summary suspensions in those cases where evidence is presented that convinces the Board there is immediate danger to the public, the Board recently has adopted the procedure of conducting immediate "show cause" hear-

ings in advance of using the summary suspension power whenever possible.

In addition, as a result of criticism from the physician community regarding summary suspension actions being reported in the media prior to physicians being personally notified, the Board has adopted a policy of notifying the physician by telephone immediately after issuing a summary suspension. Since the Medical Licensing Board hearings are routinely covered by the media, and are subject to the open-door law, it is impossible to guarantee that in all instances physicians can be contacted prior to the story breaking in the media; however, the Board is sensitive to this concern and is doing everything in its power to see that this does not happen.

Complaint Processing

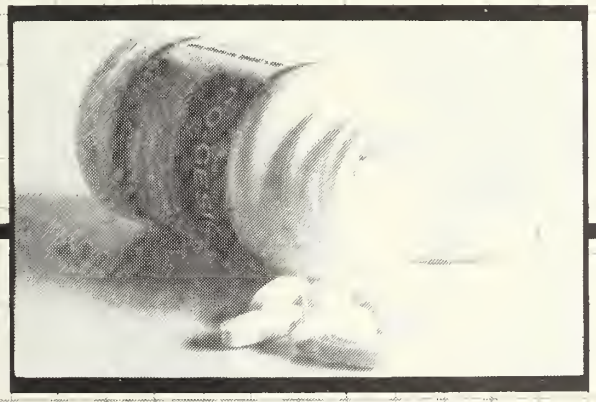
By statute, the director of the Division of Consumer Protection, which is a part of the Attorney General's office, receives, investigates, and prosecutes complaints concerning all regulated occupations. Currently, the Attorney General's office has assigned to the Medical Licensing Board several attorneys who specialize in the prosecution of physician complaints before the Medical Licensing Board, and they have developed great expertise in that area.

All complaints are required to be in writing, signed by the complainant, and initially are filed with the director of the Division of Consumer Protection of the Attorney General's office. The statute provides that any person may file a complaint, including members of any of the health profession boards. The director of the Consumer Protection Division of the Attorney General's office has the power to make an initial determination as to the merit of a complaint. If he concludes that the complaint has merit and should be submitted to the Medical Licensing Board, the Board thereby acquires jurisdiction over the matter.

In addition, the Attorney General's office, through reasonable means, must notify the physician respondent of the nature and ramifications of the complaint and of the duty of the Medical Licensing Board to attempt to resolve the complaint through negotiation, if possible.

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PREMENSTRUAL SYNDROME
A Critical Review of the Literature

ANITA D. SPITZ
Indianapolis

TO SOME, Premenstrual Syndrome (PMS) is one of the "world's most common diseases."[1] To others, it is a way of keeping a woman "in her place" and should not be classified as a disease at all.[2] To most, it is a non-issue.[3] No matter what one's position may be, the issue of PMS is making a significant impact within the legal profession. And, as an offshoot of that legal interest, PMS is becoming a concern among the general public. The more widespread such interest grows, the more affected professionals will need to understand the condition and be able to deal with it.

This paper will present a review of the extant literature on PMS with respect to its definition, causes, diagnosis, treatment, and the exploitation of PMS as a defense for criminal behavior. Indications as to the future course of PMS within the medical and legal professions will be presented in the conclusion.

Premenstrual symptoms have been known since ancient times. Jane Trimble, president of the PMS Clinic in Minneapolis, Minn., quotes a Greek writer, Semonides, who once penned, "one day she is all smiles and gladness . . . , but the next, she is dangerous to look at or approach. . . ."[4]

The author is a senior medical student at Indiana University School of Medicine, Indianapolis.

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Apart from Semonides' perceptive observations in ancient Greece, few learned men did much more about such feminine caprice than to just live with it. It wasn't until 1931 that one Dr. Robert Frank investigated what he called Premenstrual Tension. Frank set forth what have become the classic symptoms of PMS. He diagnosed PMS sufferers as exhibiting edema, weight gain, feelings of restlessness, irritability and "indescribable tension."[5]

In 1938, Frank's observations were expanded by one Dr. S.L. Israel. He determined that Premenstrual Tension (the early term for PMS) produced striking personality changes, but cautioned observing physicians to look carefully into each psychotic episode to make certain that a patient might not have a more serious illness.[6]

Between 1938 and the 1950s, little else was written on PMS. Then, in 1953, Dr. Katharina Dalton, founder of the world's first PMS clinic and currently the leading authority on PMS, presented a paper on the subject. She, along with her co-author, Dr. R. Greene, coined the phrase "Premenstrual Syndrome" and defined the criteria for PMS. These criteria are that a patient must have symptoms in the second half of the menstrual cycle and a symptom-free period of at least seven days in the first half of the cycle.[7] In a following article, Dalton later added the provisions that symptoms must occur in each of three previous cycles and must be severe enough to demand medical advice or relief.[7] She has continued to proffer these original diagnostic criteria almost unchanged for the last 30 years.[1]

Much research has been performed on estimating the numbers of sufferers.

A 1986 PMS Study Showed That 20-40% of All Women Have Mental or Physical Incapacitation and That 90% Suffer Recurrent PMS Symptoms

Between 1953 and 1957, there were 10 reported studies calculating the range of sufferers anywhere from 15% to 95% of the female population.[7] Other studies followed. The most current study was performed in 1986 by Dr. Thomas Riley, a family practitioner in Pasadena, Calif. He determined that 20-40% of all women have mental or physical incapacitation and 90% suffer recurrent PMS symptoms.[8]

Etiologic theories vary as widely as the estimated number of sufferers. Frank deduced that PMS was caused by a build-up of excess estrogen due to a decrease in renal excretion.[4] Israel believed that an excess of unantagonized estrogen from defective ovarian leutinization secondary to a decrease in progesterone brought about the symptoms.[9] Dalton claimed an altered estrogen-progesterone ratio to be the culprit.[9] Other studies supported hormonal and electrolyte imbalances resulting in water retention.[7] Even

others claimed carbohydrate metabolism as a possible cause, that PMS was the result of hypoglycemia.[7] More recent studies indicate neuroendocrine factors. Doctors R. Reid and S.S.C. Yen, faculty members of the Obstetrics and Gynecology (OB-GYN) Department of the University of California School of Medicine, maintain that the hypothalamic and pituitary axis involving an increase in prolactin or prostaglandins is the basic cause of PMS.[10]

All of those studies are questionable. The concept of water retention was refuted by Dr. Irwin Perr of the Cleveland Regional Treatment Center, soon after that possible cause was presented. Perr provided evidence that water retention was not a consistent finding in PMS. His study sample included PMS sufferers without edema and others with water retention showing no significant emotional changes. He also attacked the hypoglycemia hypothesis with clinical research indicating that hypoglycemia was only a reflection of and not a causative factor in PMS.[7] No study countering neuroendocrine factors has surfaced to date, but the etiology is far from settled. Reid and Yen and others are continuing their research.[11] In addition to the theories presented above, there are others encompassing sociobiologic, social, psychosocial and biological causes.[12]

Currently accepted symptoms associated with PMS as a result of the wide latitude allowed by the etiology are rather broad. Those symptoms range all the way from mild discomfort and irritability to severe gastrointestinal illness and gross personality changes. In all, there are more than 150 symptoms relating to PMS.[1] The key factor to all symptoms is a periodic recurrence. These symptoms must begin 10-14 days before menstruation and continue for several days. This allows for the incorporation of personal opinion into the diagnosis of PMS much more so than for other afflictions.

Treatment of PMS is almost as varied as the symptoms. Frank recommended calcium lactate for sedation, caffeine as a diuretic, and magnesium citrate as a laxative.[4] Dalton continues to advocate natural progesterone. This is the most utilized treatment for severe PMS, but is not an accepted treatment in the United States.[1] Dr. Cynthia Cook, Assistant Professor of OB-GYN at the University of Pennsylvania School of Medicine, administers a regimen of reassurance and specific symptom treatment.[13] Other less-popular treatments, including a variety of home remedies, exist.

These PMS treatments have been the subject of much discussion in medical journals. Dr. Kay Heggestad, a family practitioner and a graduate of the University of Wisconsin Medical School, claims that the placebo effect of any treatment can be as high as 40-60%.[14] Dr. Dalton defends her treatment by alleging either misdiagnosis or incorrect dosage if there is no improvement in the PMS sufferer receiving progesterone within three months.[1] Dr. Louis Keith, of the Northwestern University School of Medicine, contends that the progesterone treatment is unorthodox and recommends against it.[13] Dr. Georgeanna Jones, of the Eastern Virginia Medical School, found no improvement with progesterone treatments in a clinical study and questions the regimen.[13] Dr. Elizabeth Gonzales, in an article published in the *Journal of the American Medical Association*, questions Dr. Dalton's research methods indicating progesterone treatments as a possible treatment.[13]

Such controversy with PMS would affect few outside of the medical profession, except that there have been attempts to link PMS with extreme feminine behavior because of the occasional psychosis present in PMS sufferers. In 1945, Dr. Cooke asserted that most crimes committed by women in Paris occur during their menstrual period.[8] Dr. J.H. Morton, in an article published in the *American Journal of OB-GYN*, determined that 80% of 249 female prisoners in a volunteer study suffered from PMS.[7] Dalton claimed that as many as 52% of a study group suffered accidents during or at least four days prior to menstruation.[15] Dr. M.I. Whitehead, a one-time lecturer in the Department of OB-GYN at Kings College Hospital Medical School in London, alleged in an article published in the *British Medical Journal* in 1934 that airplane crashes involving women pilots were the result of menstruation.[15]

THE ISSUE OF PMS IS MAKING A SIGNIFICANT IMPACT WITHIN THE LEGAL PROFESSION—AND IT IS BECOMING A PUBLIC CONCERN

Dalton claimed a more specific relationship between anti-social behavior in women and the menstrual cycle in additional studies. She alleges that PMS sufferers display an increase in aggression and a corresponding increase in criminal behavior before menstruation.[16] Doctors Morton and Paul d'Orban concurred with Dr. Dalton in a study indicating that feminine violent crime appears to be related to menstrual cycles.[17] At the same time, those two men cautioned that such periodic aggressive behavior seems to be restricted to already unstable women.[17]

In keeping with those findings, the phenomenon of PMS was officially recognized as a contributing factor in diminished mental responsibility in

England with the Homicide Act of 1957.[7] There is also a history of successful court room defenses of female offenders based upon diminished mental responsibility prior to the medical investigation of PMS in England. One woman was acquitted of shoplifting in 1845 and two women were acquitted for murder in 1851. In each case, temporary insanity as a result of "suppression of menstruation" was alleged.[1]

Two more recent cases using a PMS defense have been tried in the British courts. The first case, *R v. English*, involved a 37-year-old woman charged with the murder of her lover. A charge of manslaughter, based upon diminished responsibility resulting from PMS, was adjudged.[18] The other case, *R v. Craddock*, involved the retrial of an earlier case over the stabbing death of one woman by another. The defendant received a reduced charge of manslaughter due to diminished responsibility as a result of PMS.[18] In both instances, expert testimony was provided by Dr. Dalton.

Even Though PMS Has Been Linked with Insanity and Diminished Responsibility, Should It Be Used as a Legal Defense for Criminal Behavior?

Courts in the United States, on the other hand, have failed to accept PMS as a defense. Still, PMS-related defenses have been attempted. One recorded case was successful while two were not. In *Reid v. Florida Real Estate Commission*, a 49-year-old woman was acquitted of a minor theft based upon diminished responsibility as a result of PMS.[19] Expert testimony was provided by her physician and a psychiatrist. In *ReLovato v. Jamie Lynn Irvin*, a murder trial, a plea of diminished responsibility was rejected based upon expert testimony. The court found no "general acceptance of PMS in psychiatry as an explanation for inappropriate behavior."[20] In *People v. Santos*, a case of maternal child abuse, a plea of diminished responsibility was rejected by the bench.[21]

These cases are controversial. Numerous articles have appeared in legal journals both supporting and condemning the use of PMS as a defense for feminine criminal behavior.

An English barrister, Diana Brahms, has spoken out against the practice of accepting PMS as a mitigating factor in feminine criminal behavior in England.[18] She fears that such largess may pave the way toward further liberalization of the definition of diminished responsibility. Similar views appear in other English publications.[22,23]

Some American journal articles present a like appraisal of PMS-related defenses. In 1953, H. Oleck, writing in the *International Record of Medicine*, argued against the incorporation of PMS within the concept of diminished mental responsibility.[7] In 1958, Irwin Perr declared that a diagnosis of PMS does not have any importance when evaluating mental status.[7] Marc Press, a contributor to the *Duke Law Journal*, wrote, "No scientific evidence indicates that PMS alone can produce psychosis, thus [there is] little hope [that] an insanity defense . . . would succeed."[17]

At the same time, other articles have recently appeared in favor of limited use of PMS-related defenses. Barbara Clay, an attorney published in the *Women's Law Journal* in 1984, argues for the possibility of utilizing a plea of diminished responsibility in the case of severe PMS sufferers, but sees little recourse for the mild sufferer.[19] Richard Oakes, former dean of Hamline University School of Law, suggests that PMS can be a successful mitigation tool as long as it insures no precedent is set, no new insanity or intent definition is created, and no statute or case is overturned.[24]

The majority of legal argument was incorporated into statute in the United States with the Insanity Defense Reform Act of 1984 [18 U.S.C.A. § 20 (Supp. 1985)].[24] That statute provides that PMS may be argued as a mitigating factor in criminal behavior if it is connected with a psychosis.[24] That legally links PMS with insanity, diminished responsibility, diminished capacity, and automatism. Any defense based upon PMS in the U.S. federal courts must prove the defendant incapable of forming a specific state of mind at the time of the offense. Robert Carney and Brian Williams, then third-year law students, discuss and defend just such a statute in the *Notre Dame Law Review* of December 1983.[21]

Articles discussing the use of PMS-related diminished responsibility defenses have flourished. Arguments both for and against such a defense have been raised. Barbara Clay writes that the PMS defense in *People v. Santos* was flawed in that the abuse was a crime of specific intent and should not set precedent in future cases.[19] She included an interview with Dr. Dalton where Dalton diagnosed Santos as not suffering from PMS, as a key argument in her essay. Richard Oakes refined Clay's arguments further to include the premise that PMS-related evidence should be dependent upon expert medical testimony rather than legal definition.[24] Carney and Williams concur with Clay and Oakes, but argue for an interim definition since PMS sufferers have already and may continue to be imprisoned unjustly.[21] Other articles offer minor variations of the above.

Many articles deal with the possibly negative consequences of PMS-based arguments in the courts. Kay Heggestad wonders if "perhaps it could be assumed that if murder is committed, it must be severe PMS."[14] Carney and Williams raise the issue of a PMS-related defense being sexist.[21] Elizabeth Gonzales questions whether the spectre of PMS might be used to restrict a woman from holding political office, obtaining a pilot's license or even obtaining custody of her children in divorce cases.[13] The following appeared in an editorial in the *New York Times* of March 7, 1986: "Women have as much control over their lives and actions as men do . . . To use PMS as a legal defense would be a giant step backward."[25]

Some articles have supported the concept of a PMS-related defense for female defendants. Doctors d'Orban and Dalton continue to defend the linkage between PMS and violence in emotionally unstable women.[16] Dr Dalton contends that a PMS defense is justifiable and that any malingerers would be easily weeded out so that severe PMS sufferers could be judged accordingly.[1]

Medical researchers and interested lawyers have suggested possible directions for PMS-related litigation. Richard Oakes criticizes the legal profession for not reacting quickly enough.[24] Eira Caryl-Thomas, an English barrister, argues for confining PMS defenses within the framework of diminished responsibility.[22] Dalton encourages further expansion of PMS-related defenses in the courtroom, arguing that any PMS sufferer should not be "denied the defense merely for lack of a prior criminal record."[8] Dr. Ervin Nichols, Director of Practice Activities at the American College of OB-GYN, discourages such defenses claiming that no scientific evidence supports "any relationships between PMS and criminal behavior."[20] Dr. Riley thinks PMS is an actual affliction and it should be introduced in the courtroom as a mitigating factor in feminine criminal behavior.[8]

Some authors have dealt with specific concerns of such litigation. Carney and Williams caution against the legal profession accepting PMS as a disease while the medical profession is divided.[21] Riley ponders other concerns in his article. He lists the following, as yet, unanswered questions:

- What if the woman doesn't obtain the court ordered treatment?
- What if the treatment isn't FDA approved?
- What about side effects?
- What if a woman commits another crime while under therapy?
- Who is responsible if a physician does not diagnose or treat PMS and a woman commits a crime?"[8]

One result of all the controversy over PMS is that insurance companies are becoming involved capriciously. Without medical definition and treatment to rely on, insurance companies are arriving at policy based upon worst-case scenarios. Minnesota Blue Cross/Blue Shield has refused to cover PMS treatments if a woman is diagnosed prior to obtaining coverage; in effect, defining the condition as a disease.[4]

That is the cart-leading-the-horse effect that some concerned authors have expressed. The ramifications of such policies have yet to be thoroughly analyzed.

Interest continues to grow within the medical profession. Dr. Marshall Smith, a practicing OB-GYN physician and the former director of a PMS clinic, has said that the concept of PMS being a disease is gaining acceptance by newly graduated residents. The American College of Obstetricians and Gynecologists is actively pursuing patient education on the topic. Several drug companies have issued PMS information pamphlets. Research into a specific etiology continues.[11] If the cause of PMS can be discovered, then a specific and effective treatment might be forthcoming.

Interest in the legal aspects of PMS continues to grow. This is because various members of the legal profession continue to pursue acceptance of a PMS-related defense for some feminine criminal behavior. As a result of those efforts, legal journals continue to carry PMS articles. The *Hamline Law Review* recently devoted a large section of one issue to PMS.[26]

WITHOUT MEDICAL DEFINITION AND TREATMENT TO RELY UPON, SOME INSURANCE COMPANIES ARE MAKING POLICY BASED ON WORST-CASE SCENARIOS

While this professional interest grows, public awareness and interest in both the medical and legal aspects of PMS have lessened. Dr. Smith offered Phoenix as an example of that trend. In 1980, ten local PMS support groups existed in that city. Today, although some PMS sufferers still seek treatment, only one PMS support group exists, and all the PMS clinics have closed.[11] Dr. Smith believes PMS sufferers are discouraged by the lack of any improvement in PMS treatment. However, public interest could easily be revived by either a medical breakthrough or a favorable courtroom decision.

Therefore, it remains difficult to make any assumptions concerning the future of PMS. Arguments both for and against the effects of PMS, its various treatments, its use as a defense in the

courtroom, and medical insurance liabilities all have merit. Those interested in PMS should be aware that, even today, as has been the norm over the past 50 years, there is much opinion and little consensus.

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Indiana's Congressional Delegation

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Sen. Dan Quayle (R)—Hart Senate Office Bldg., Room 524, Washington, D.C. 20510—(202) 224-5623.

Rep. Pete Visclosky (D-Dist. 1)—420 Cannon House Office Bldg., Washington, D.C. 20515—(202) 225-2461.

Rep. Phil Sharp (D-Dist. 2)—2452 Rayburn House Office Bldg., Washington, D.C. 20515—(202) 225-3021.

Rep. John Hiler (R-Dist. 3)—407 Cannon House Office Bldg., Washington, D.C. 20515—(202) 225-3915.

Rep. Dan Coats (R-Dist. 4)—1417 Longworth House Office Bldg., Washington, D.C. 20515—(202) 225-4436.

Rep. James Jontz (D-Dist. 5)—1005 Longworth House Office Bldg., Washington, D.C. 20515—(202) 225-5037.

Rep. Dan Burton (R-Dist. 6)—120 Cannon House Office Bldg., Washington, D.C. 20515—(202) 225-2276.

Rep. John Myers (R-Dist. 7)—2372 Rayburn House Office Bldg., Washington, D.C. 20515—(202) 225-5805.

Rep. Francis McCloskey (D-Dist. 8)—127 Cannon House Office Bldg., Washington, D.C. 20515—(202) 225-4636.

Rep. Lee Hamilton (D-Dist. 9)—2187 Rayburn House Office Bldg., Washington, D.C. 20515—(202) 225-5315.

Rep. Andrew Jacobs Jr. (D-Dist. 10)—1533 Longworth House Office Bldg., Washington, D.C. 20515—(202) 225-4011.

Snakeroot Extract

Number 9 April, 1987

A NEWSLETTER OF INDIANA MEDICAL HISTORY

Society Receives Administrative Records of Planned Parenthood

Planned Parenthood of Central Indiana recently agreed to deposit its administrative records at the Indiana Historical Society Library. These records consist of minutes of local board meetings from the 1930s to 1980 and correspondence and other administrative records from the late 1970s. According to the agreement reached with Planned Parenthood, the organization will donate additional administrative records to the Society as these records become unnecessary for current business. The records are important sources for the study of the birth control movement in Indiana as well as the changing role of women in society.

The local chapter of Planned Parenthood started in 1932 as part of a larger birth control movement in the United States (see related article on page 2). Originally known as the Indiana Birth Control League, the organization changed its name in 1934 to the Maternal Health League. Although in the 1910s, the Indianapolis public had supported the nascent birth control movement, by the 1930s Planned Parenthood found its audience much less amenable to the cause. Particularly controversial was the establishment of a birth control clinic in Indianapolis in 1933. Much controversy centered on who would be admitted as patients to the clinic. As a result of pressure from both the public and the Indiana Medical Society, a very restrictive admission policy was adopted. Whereas most birth control clinics accepted any married woman, the Indianapolis clinic decided to admit only poor, married mothers of at least two children who had been referred by a licensed doctor or "recognized social agency." Operating on a shoestring budget and primarily with a volunteer staff, this clinic provided medical services and birth control counseling to its patients. Yet, given these stringent guidelines, attendance during the early years of the clinic was low.

In the 1940s and 1950s the organization expanded its membership and services and controversy continued. By the 1960s services offered by Planned Parenthood included premarital counseling, marriage success seminars, and infertility services. The largest growth in the organization came with FDA approval of the first oral contraceptive in the early 1960s. Although the organization is now well established in the community, it continues to be controversial as it takes a central role in the current debates over abortion and birth control counseling for teenagers.

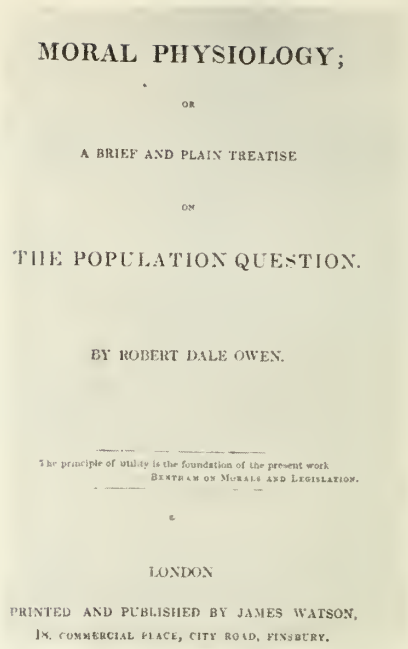


Planned Parenthood advertisement, 1978. In the collection of the Indiana Historical Society Library.

A History Of The Birth Control Movement

On May 15, 1916 birth control advocate Margaret Sanger addressed "a vast crowd of women" in the old Claypool Hotel in downtown Indianapolis. Although a controversial individual, Sanger was well received by her audience. When a few individuals at the meeting spoke out against birth control practices, the women "hooted, hissed and ridiculed [them] with penetrating female giggles." In contrast, when Sanger spoke she drew "long and prolonged applause." Although strong opposition to the birth control movement later developed in Indianapolis, in 1916 many of the city's women seemed in favor of Sanger's ideas on family planning.

As revolutionary as the birth control movement was in 1916, the concept of consciously limiting the size of the family was not new. In 1831 Robert Dale Owen (1801-1877), son of the founder of the Utopian socialist community at New Harmony, Indiana, published the first important American tract on birth control. Although his book, *Moral Physiology; or a Brief and Plain Treatise on the Population Question,* was primarily an essay on social science, it did contain a brief discussion of various birth control methods available at the time. Those methods propounded by Owen included the vaginal sponge, the condom (which at that time was made from the intestine of sheep and only available by importation from Europe), and withdrawal. Others at the time recommended douching with a spermicide. With the development of the vulcanization of rubber in the 1830s and 1840s, the technology was in place to produce inexpensive rubber condoms and by the 1850s the production of "questionable rubber goods" was a booming business. In 1864 Dr. Edward Bliss Foote introduced a primitive diaphragm which he called the "womb veil." Whether the public consciously practiced birth control using the various devices on the market or whether they merely repressed their sexual desires is debatable. What is evident, though, is that by mid-century, fertility rates had declined drastically. In 1800 the average American woman bore 7.04 children. By 1860 that number had dropped to 5.21 and by 1900 to 3.56.



MORAL PHYSIOLOGY;

OR

A BRIEF AND PLAIN TREATISE

ON

THE POPULATION QUESTION.

BY ROBERT DALE OWEN.

The principle of utility is the foundation of the present work
BENTHAM ON MORALS AND LEGISLATION.

LONDON

PRINTED AND PUBLISHED BY JAMES WATSON,
18, COMMERCIAL PLACE, CITY ROAD, FINSBURY.

Frontispiece of Robert Dale Owen's Moral Physiology, the first American tract on birth control. Book in the collection of the Indiana Historical Society Library.

This relatively "open" atmosphere concerning birth control techniques ended after the Civil War with the beginning of a moral reform movement. In the 1870s the systematic suppression of birth control information began. It culminated in 1873 with the passage in Congress of the Comstock Act which defined birth control information as obscene and made the dissemination of it a violation of federal law. Even doctors who had formerly supported contraception began speaking out against it.

Federal legislation was not effective in stopping the spread of birth control information. Beginning in 1906 American anarchist Emma Goldman spoke out in favor of birth control. Goldman's interest in the subject stemmed from her experiences as a public health nurse working with poor immigrant women. Her interest in birth control, however, was short-lived. In 1912 Margaret Sanger (1883-1966) became the leading proponent of the movement. It was because of Sanger's strong leadership and devotion to the cause that the birth control movement succeeded. Sanger, like Goldman, had been a public

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Snakeroot Extract is a joint publication of the Indiana Historical Society's Medical History Committee (315 West Ohio Street, Indianapolis, Indiana 46202) and the Indiana Medical History Museum (Old Pathology Building, 3000 West Washington Street, Indianapolis, Indiana 46222). The newsletter is mailed to members of both the committee and the museum.

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Submit all items for publication in the newsletter and inquiries about membership information to the Managing Editor, c/o Indiana Historical Society, 315 West Ohio Street, Indianapolis, Indiana 46202.

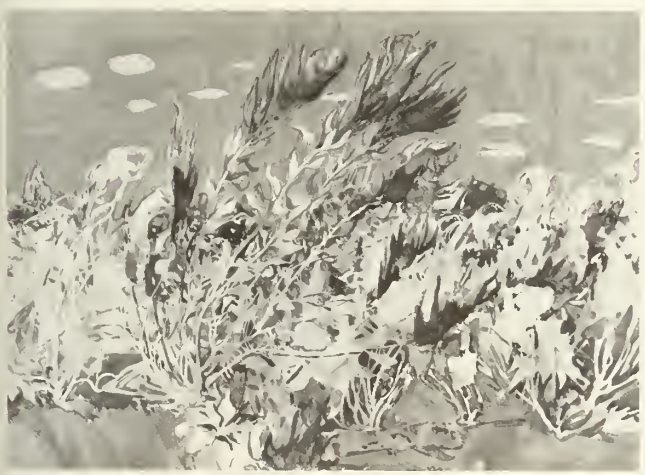
Snakeroot Extract derives its name from the white snakeroot plant, a plant that is significant in Indiana medical history. For years, a mysterious disease called milk sickness plagued early Hoosiers. There were many theories as to the disease's cause, but the actual cause remained unknown until the 1920s. At that time, the disease was traced to the white snakeroot plant or, rather, to the consumption of milk from cows that had eaten it. The plant contains the poison tremetol.

Museum Participates In Arts Touring Program

The Indiana Medical History Museum will be participating in the Indiana Arts Commission Presenter/ Touring Program for 1987-88. This program is designed to facilitate the presentation of high quality art in Indiana and increase the visibility and financial support of art groups and exhibitions. As a participant in this program, the museum will make available to art galleries and museums across the state an exhibition of sixteen masterfully executed watercolors by John Zwara. Zwara's paintings are in the collections of the Indiana Medical History Museum.

Zwara was a patient at Central State Hospital in 1938. Although most of the details of his life remain a mystery, admission records to the hospital indicate that he was born in Austria in the early 1880s and came to America in 1900. Zwara had no family and very few friends in Indianapolis. Sleeping in the streets and subsisting off a diet of bread and coffee, Zwara earned money for his supplies and meager diet by selling his paintings to Lyman Brothers and the H.L. Leiber Company in Indianapolis. Zwara was eventually befriended by Alexander Vonnegut who recognized Zwara's remarkable skill with watercolors, as well as his need for psychiatric help. Vonnegut had Zwara committed at Central State Hospital. At the hospital Zwara was diagnosed as schizophrenic, but was given the freedom to paint. Walter Bruetsch, the hospital's pathologist, bought Zwara the supplies he needed. Zwara was a prolific painter, producing over ten paintings a week. He stayed only six weeks at the hospital and then escaped. He was taken in by the Little Sisters of the Poor and died while under their care in the 1940s.

A description of this traveling exhibit will be listed in the Indiana Arts Commission Presenter/Touring Directory to be published this spring. Any organization wanting to sponsor this exhibition can apply to the Indiana Arts Commission for funding. For more information contact Katherine McDonell, Indiana Medical History Museum, Old Pathology Building, 3000 West Washington Street, Indianapolis, Indiana 46222 (317/635-7329).



Watercolor by artist John Zwara



Watercolor by artist John Zwara

Birth Control Movement

(continued from Page 2)

health nurse and had seen how frequent pregnancies kept families poor and women confined to the home. When one of her patients died after attempting to terminate an unwanted pregnancy, Sanger decided to devote her life to the emancipation of women. She saw the limitation of family size the key to women's freedom. Sanger started a newspaper, *The Woman Rebel,* to circulate information about birth control. Sanger's brash assertion that women should "look the whole world in the face with a go-to-hell look in the eyes" defiantly taunted opponents of the movement. In 1914 Sanger prepared the pamphlet *Family Limitation,* which presented detailed information about contraception. Sanger mailed her pamphlet, fled the country, and remained in Europe about a year to avoid arrest. When she returned to New York, Sanger was indicted, but the publicity on the case had made her a local hero and the case was dismissed before being heard by a federal grand jury.

From 1914 to 1937 Sanger worked to convince the middle class, legislators, and the medical profession of the importance of birth control. To accomplish this, in 1921 Sanger organized the American Birth Control League, a national organization designed to promote the cause. In violation of the Comstock Act, she opened birth control clinics across the country and conducted research on the effectiveness and safety of various contraceptive devices. Through these clinics, Sanger popularized the use of the spring-loaded diaphragm. Her work

(continued on Page 4)

(continued from Page 3)

at these clinics and her persistent efforts to educate women about birth control led to the formal recognition of contraception as a legitimate part of medicine in 1937. Through a variety of court cases, she also took the edge off the Comstock Act. (It was not until 1970, however, that Congress completely reworked the law and removed birth control devices from the obscene list.) Ironically, much of Sanger's support came from the middle class, which was alarmed at the seemingly high fertility rate of the immigrant classes and wanted to limit these births.

From the late 1930s through the 1940s, Sanger lived in semiretirement. Her crusade to spread information about contraception had almost been too successful. For the first time, America's birth rate had fallen below replacement level. The survival of the birth control movement meant the organization would have to adapt to a new environment. In 1942 the title of the national organization changed from the Birth Control Federation of America to the Planned Parenthood Federation of America, although Sanger despised the name 'planned parenthood' and felt it disguised the true purpose of the organization. She felt that large numbers of people should have no children.

Nonetheless, in the late 1940s Sanger decided to work for Planned Parenthood. She believed that although much had been accomplished, there were still millions of women in third world countries and many poor American women who could benefit from birth control information. Yet, Sanger and many others realized that widespread use of birth control awaited breakthroughs in contraceptive technology. These advances did not come until the 1960s when the IUD and oral contraceptives were placed on the market. These two developments finally made birth control readily available to the masses and dramatically altered the role of women in society.



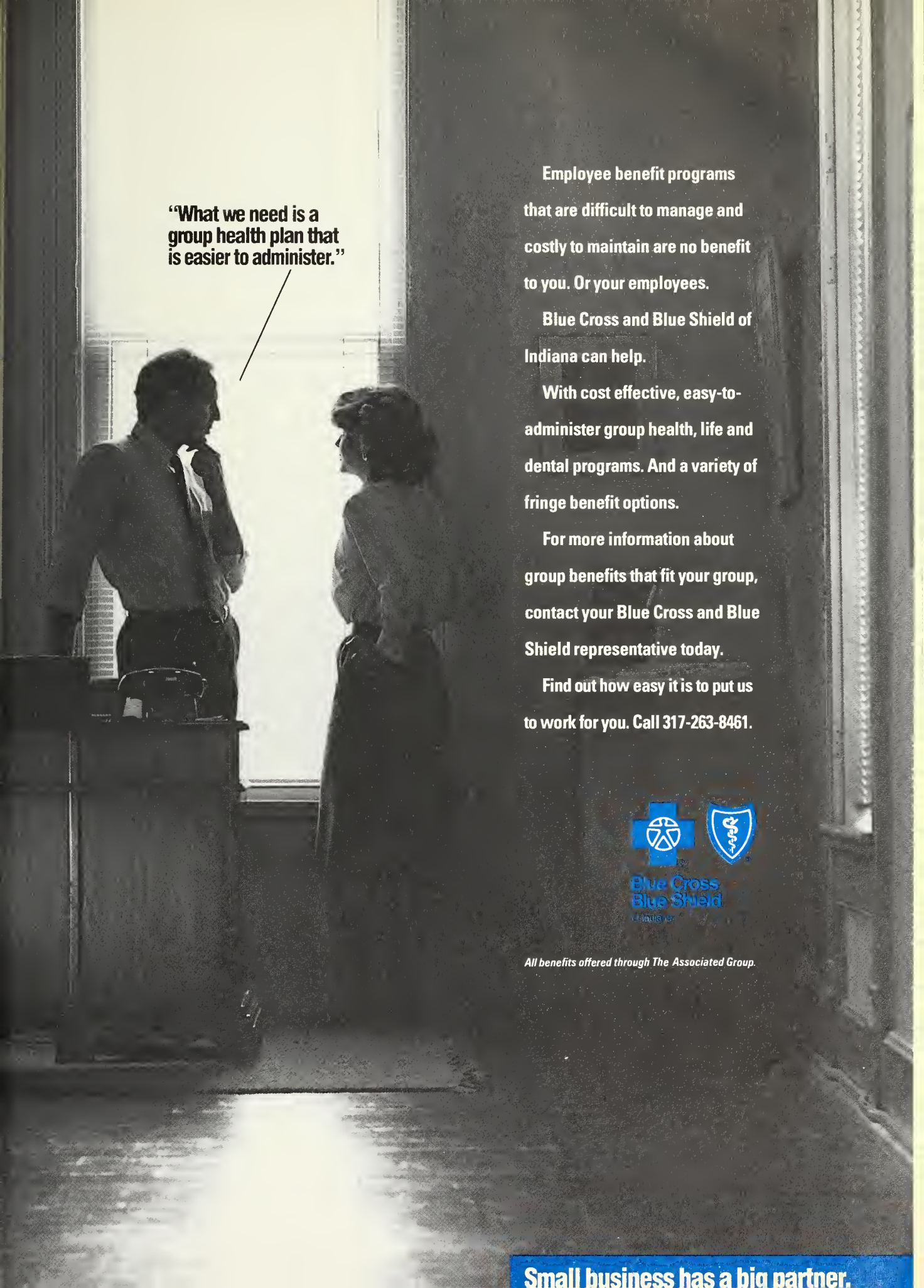
Noted Woman Birth Control Advocate
Who Will Speak at Conference Today

[Copyright, 1916, Underwood & Underwood.]

Mrs. Margaret Sanger of New York city, the advocateer of birth control, will speak to the National Conference of Charities and Correction members at the Claypool Hotel this afternoon. Mrs. Sanger was indicted by the Federal Grand Jury for spreading her views broadcast. She was freed before the case was submitted to the jury. She says the poor woman with a large family needs the message of birth control.

Margaret Sanger. Taken from the Indianapolis Star, May 15, 1916.

Indiana Historical Society
Indiana Medical History Committee
315 West Ohio Street
Indianapolis, IN 46202



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Commentary

VICTOR J. VOLLRATH, M.D.
Indianapolis

SMOKING IS A "grave" matter. Light up! Your coffin may be dark. This commentary is not just another article on hazards of smoking. It is one that bitterly denounces the "breathtaking" habit, especially as practiced on commercial airlines. I am adamantly paranoid in my opposition to smoking tobacco while flying. This issue was recently brought to my attention again during a vacation trip. I also will relate an incident in general practice that ended in a serious cigarette-caused fire at my home.

I have had a busy general practice in a suburb of Indianapolis for 40 years. Nearly 20% of this practice has been as an active medical examiner for the Federal Aviation Agency. I am also company physician for the local American Trans Air airlines and its subsidiary "AmbassadAir." This is a worldwide air travel club, one of the largest. Aviation Medicine has been not only a vocation, but also an avocation, a first love, in my life.

Before explaining why I believe cigarettes should be banned on airlines, you should first know why I am fearful of cigarette fires.

Ten years ago, my office was in my home. I had built a double house. My residence was on one side of the double, my office on the other.

One hot August night, about one o'clock, the telephone rang. An excited housewife, living one block from my office, frantically told me her husband had been eating a Dagwood sandwich at the kitchen table when he turned gray and fell to the floor. I quickly told her to perform the Heimlich Maneuver, to give him strong repeated bear hugs with her fists in the pit of his stomach. This was the most unusual house call I ever made, dressed only in my house slippers, pajamas and bath robe. It was also the fastest call I ever made. I ran to the garage. My car windows were already down. I was parked at the patient's home in less than a minute.

The 40-year-old man was still on the kitchen floor but, thank God, he was breathing. His wife said when she gave him the first strong hug, out popped an olive. Her husband had a habit of treating his insomnia by raiding the fridge. I checked his throat, heart, lungs and blood pressure. They all seemed to be satisfactory. I helped him back to bed and waited a while to make sure his vital signs remained stable. I advised him not to eat in the future when he was half asleep.

I returned to my car thankful but exhausted. The car windows were still down as I drove home. I thought I noticed a strange odor in the car, but at two o'clock in the morning, my only interest was in getting some "shut eye." I had the car back in the garage, next to my wife's new Oldsmobile, about as quickly as I had left. I was soon sound asleep.

It was about 3:30 a.m. when my wife awakened me to the terrible sound of burning timbers. Flames were 10 feet in the air above our garage. The fire department came quickly and prevented the fire from spreading to the house. The fire chief and I both are convinced that a passing motorist casually had flipped a cigarette, and it landed on the rear cushion of my Cadillac while it had been parked in front of the patient's house. The odor I had noticed must have been a smoldering rear cushion. Both cars were totally destroyed.

The next day, I removed all ashtrays from my office waiting room and requested that no employee smoke while on duty. I put "Thank You for Not Smoking" signs in my waiting room. This decision really helped my practice. The office air pollution was eliminated and my patients thanked me for it. I am convinced that the airlines would also be aided by such a step.

Recently, the U.S. Army banned smoking in many areas of its installations. Eli Lilly and Company now forbids smoking in all its working areas. Many other institutions and hospitals are banning tobacco. If such famous organizations are objecting to smoking on the ground, why are the airlines hesitant to join forces in the air?

This brings me now to my point about smoking aboard commercial airliners. My story involves one of the happiest weeks of my life, the first week in August 1986.

American Trans Air had generously furnished me four seats on their six-day tour to Seattle. My wife and I in-

vited my younger brother and his wife who live in another state, and whom we seldom see, to join us. It was fun being with them and, as it turned out, this was the only vacation I have ever taken that was perfect.

Our Boeing 727 flight left Indianapolis at eight o'clock Sunday morning. Within three hours we were flying over the snow-capped Rocky Mountains. The pilot started his descent as we passed Mt. Ranier, 65 miles south of Seattle. This mountain was a beautiful sight because the sun was out, and we appeared to be only a few miles away. As we passed this area, I thought of Victor Borge who said, whenever he boarded a plane, he always took the back seat because whoever heard of a plane backing into a mountain?

I have no fear of flying, even over the mountains. I did, however, have a strong apprehension knowing that at the rear of the plane was a happy group of travelers enjoying the "luxury" of smoking.

Less than four hours from home, we landed at the Seattle-Tacoma Airport. It was only 10:40 in the morning, temperature 72, and the day was beautiful.

I would like to mention a few trip highlights in order to stress a point. The issue I want to emphasize is that man is a paradox. God has given him aviation, the same as He has given him electricity—to use, to enjoy, and to respect. Man is intelligent enough to travel in space. We put an automobile and two men on the moon. The paradox of man is that he is brilliant enough to make the skies practically unlimited to aviation, but he is stupid enough to play Russian Roulette by permitting smoking sections on airlines. I hope the time is near that the authorities realize oxygen carried on airplanes is highly vulnerable to matches used by passengers.

In Seattle, we checked in at the Four Seasons Olympic Hotel. The accommodations were exquisite. We spent three days touring sights in and around Seattle. The scenery was gorgeous, and the weather was ideal.

The most interesting portion of the Seattle area was a tour of the Boeing Commercial Airplane Company at Everett, Washington. This one huge building is 11 stories tall and covers 62 acres. Here they make 747 and 767 airplanes like Detroit makes Lincolns and Cadillacs. It was amazing. Bill Boeing, its founder, was certainly an aviation giant.

We spent the remaining three days of our trip at Expo '86, the World's Fair at Vancouver, Canada. I have been visiting world's fairs since 1932 and Expo '86 was by far the best I have ever seen. There were more than 80 pavilions and exhibits of countries throughout the world. Time only permitted us to visit about half of them.

We returned to Seattle just in time to catch our plane to Indianapolis. I have elaborated on this magnificent trip, because only by air can one travel clear across the country and see so much beauty, knowledge, and history in such a short time. Aviation has given us the privilege and the rare opportunity to realize such a perfect vacation. We should revere and respect this privilege rather than degrade and disgrace it by permitting smoking on commercial airlines.

Our flight home was again smooth, non-stop, and less than four hours. As we landed in Indianapolis I told my wife, except for my phobia of the air polluters in the rear of the plane, this had been a perfect vacation. To me smoking is a "Burning Issue"; it is Public Enemy Number One.

Much to my chagrin, just two days after our return, the headlines of our newspaper carried the picture and a story of an American Trans Air DC-10. The plane had been completely destroyed by fire shortly after landing at Chicago O'Hare. Fortunately, 320 passengers had just disembarked when fire engulfed the cabin. There was no indication of an engine fire or of an explosion. A tour group had just returned from Honolulu. My opinion is that it could have been due to a misplaced cigarette butt or ash, perhaps in a seat cushion of the plane.

'The Paradox of Man Is That He Is Brilliant Enough to Make the Skies Practically Unlimited to Aviation, But He Is Stupid Enough to Play Russian Roulette by Permitting Smoking Sections on Airlines.'

Last summer, a commercial airplane had to make an emergency landing in California because of a cabin fire. In 1985, a Canadian commercial plane flying from Miami to Toronto had to make an emergency landing in Cincinnati because of a fire started in the plane's rest room. If these incidents would occur while flying over the Atlantic or Pacific Ocean, having to ditch a 747 with 400 passengers would be an expensive price to pay for a misplaced cigarette butt or ash.

There is no limit to the devastation a cigarette can cause. I am safe in saying some of our billion-dollar forest fires are the result of careless smokers. We have photographic evidence that the space shuttle Challenger disaster was due to a very small, but misplaced, flame.

The world's most deadly recent fire, the Russian Chernobyl explosion, was

due to human error. This fire was 10 times worse than the bomb fires of Hiroshima or Nagasaki. We may not be able to control human error but much more could be done to prevent it along the lines of aviation tobacco smoke.

Disregarding smoking on airlines, Patrick Reynolds, grandson of the R.J. Reynolds Tobacco Company founder, recently said the tobacco industry has literally killed millions of people and will kill millions more unless smokers and Congress wake up. He said that cigarette smoking is costing the U.S. economy $65 billion a year in medical care and lost productivity.

The American Medical Association is to be congratulated on its most recent endeavor to seek legislation to deter the use of tobacco. However, Congress is not cooperating with the AMA. The Washington, D.C. "Kiplinger Letter" of Aug. 22, 1986 states that Congress will not consider a ban on smoking aboard domestic airlines. The reason is that they fear political tobacco-state opposition.

I would like for all who read this article to write to their Representatives and Senators concerning the demon—tobacco. Impress upon them in a nice way that we all want to live. Tell them that, of all the arts, the greatest is the art of living. Youth is a gift of God, but old age is an art. If the politicians are not persuaded by pleadings and sweet talk, then suggest they "Butt Out or Step Out at 30,000 Feet."

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AIDS: An Agonizing Problem

INCLUDED IN THIS ISSUE of INDIANA MEDICINE is a report on the recent "AIDS in the Heartland" conference sponsored by the Indiana State Board of Health. I had the opportunity to join Dr. Michael Mellinger, chairman of the ISMA Board of Trustees, and Dr. Lawrence E. Allen, past president, to host a dinner meeting for the conference's key speakers.

It became apparent during the course of the evening that AIDS has become an agonizing problem for those involved in medicine. It is a disease with long-range social, sexual, political and economical ramifications. The transmission of AIDS involves activities many people won't talk about, even in the privacy of their own homes. AIDS, more than any other disease, has the potential to transform the sexual revolution of the last 20 years. And while it is tantamount that a means be developed to cure or prevent it, in some quarters, those who have used the disease to justify arguments against certain practices and lifestyles have gained more attention.

More than $416 million was budgeted in fiscal year 1987 for AIDS research—research that is expected to continue for at least five years before a vaccine for the disease can be developed. Hospital costs for one patient for 28 days have been estimated at $98,000. Says one Indiana doctor who cares for AIDS patients, "We will be asking society, 'Do we spend money on heart transplants or on AIDS?'" Just as importantly, we will have to make some difficult decisions in terms of how we will provide quality care for AIDS patients at an affordable cost.

I was impressed with researcher David K. Henderson, M.D., of the National Institutes of Health, and Constance Wofsy, M.D., co-director of AIDS Activities at San Francisco General Hospital. Both were in the position of having seen early cases of AIDS and were able to offer appropriate suggestions on what we must do in Indiana. They are concerned not only with research efforts, but that immediate steps be taken to educate the public and to prevent the spread of the disease. Dr. Wofsy is also particularly concerned about the need to develop our system of health care for AIDS patients.

While Dr. Henderson feels that the Reagan Administration is finally offering some leadership for addressing the AIDS problem, Dr. Wofsy sees the programs developed at the state and local levels as having the greatest impact.

Indeed, we have seen the response by Health Commissioner Woodrow Myers Jr., M.D., and the Indiana State Board of Health to AIDS in Indiana. Not only have test sites been set up across the state, but many materials have been prepared to help inform both the medical community and the public about AIDS. Equally as important is the development of teaching materials on AIDS by William L. Yarber, Ph.D., of Indiana University for incorporation into the school curriculum. As Dr. Wofsy says, "We have to get to the young people whose sexual habits haven't developed yet. There isn't an alternative to education."

In-state research is taking place in Indianapolis by Robert B. Jones, M.D., and Ken Fife, M.D., who are conducting HIV antibody testing in that city's "Gay" community. In Lafayette, David Emery, M.D., and five colleagues have established two AIDS testing sites and offer treatment and counseling to those who seek it.

What remains to be done in this state is the responsibility of all of us in the medical profession. As one of the speakers at the "AIDS in the Heartland" conference so poignantly pointed out: "Sooner or later, in one way or another, this disease will touch all of us."

I have asked the ISMA staff to determine how our association can work with the State Board of Health on this weighty health problem. I would urge all ISMA members to become informed about AIDS; to be willing to share that knowledge with people in your local communities; and when faced with caring for an AIDS patient to do as Dr. Emery urged: "Make the care more human."



Shirley Thompson Khalouf, M.D.
President
Indiana State Medical Association

PRESIDENT REPORTS ON 'AIDS IN THE HEARTLAND'

AIDS: 'Medicine's Greatest Challenge'

30,000 Cases of AIDS Have Been Identified in the United States

ADELE M. LASH
Director
Public Relations

135 Cases of AIDS Were Confirmed Last Year in Indiana



"There isn't any alternative to education. We all experience conception and death, and we as a society should get over our difficulty in talking about it."—Constance B. Wofsy, M.D.

HEALTH CARE officials agree that AIDS research today is at least five years away from having an impact on the disease, and that is not a comfortable feeling. Their concern was apparent during the recent "AIDS in the Heartland" conference sponsored by the Indiana State Board of Health.

Nearly 800 persons, including doctors, nurses, and other health professionals attended the two-day conference which brought together leaders in AIDS research and patient care.

Statistically, there are now nearly 30,000 cases of AIDS that have been identified in the United States. By 1991, officials predict there will be 270,000 cases with 179,000 deaths.

The number of cases in Indiana went from 60 in 1985 to 135 in 1986. The cases are found in rural and urban counties, many of which involve patients from other states who have come home for treatment, according to Health Commissioner Woodrow Myers Jr., M.D.

Currently, there are 143 diagnosed cases, resulting in 90 deaths.

Particularly sobering is the fact that right now in Indiana the number of AIDS cases doubles every nine months (*see Table*). Health officials estimate that for every case that develops, there are 20 to 100 individuals who have the virus.

"We are focusing our work toward eradicating the spread of the virus as



"The shoe is falling and ultimately AIDS will challenge the American system of health care more than any other disease in medical history."—David K. Henderson, M.D.

the only defensible public health policy," said Dr. Myers.

An epidemiologist with the National Institute of Health sums it up this way:

"The shoe is falling and ultimately AIDS will challenge the American system of health care more than any other disease in medical history," said David Henderson, M.D.

We probably won't be able to cure those who now have or may develop AIDS anytime soon, but research to develop an AIDS vaccine is moving along, said Dr. Henderson.

Dr. Henderson's comments came following a reception and dinner sponsored by the Indiana State Medical Association for speakers at the AIDS conference.

Dr. Henderson said that while it may be as long as five years before a vaccine can be developed, "the best scientists in the country have turned their attention toward AIDS research."

Constance B. Wofsy, M.D., said that as an adjunct to the research, the country needs immediately to educate the public, especially youth, about prevention of the disease and to develop a system of "bargain basement" health care facilities where quality care can be had at a low cost.

She indicated that since avoidance of AIDS requires a change in behavior, it is absolutely critical to educate young people whose habits haven't developed. "There isn't an alternative to education," she said. "We all experience conception and death, and we as a society should get over our difficulty in talking about it."

Dr. Wofsy, co-director of the AIDS

AIDS: What Your Patients Need to Know

Acquired Immune Deficiency Syndrome (AIDS) is caused by a virus that destroys the body's immune system. The virus, called Human Immunodeficiency Virus (HIV), is fatal because it allows other infections to attack the body.

HIV may incubate in human cells for years without causing signs of illness; however, an infected person can still pass on the virus to others.

HIV has been isolated in blood, semen, breast milk, vaginal and/or cervical secretions, saliva, tears and urine. Recent studies have implicated only blood, semen and possibly vaginal and/or cervical secretions in transmission of the disease. Also, one case report indicated breast milk contaminated with HIV is a possible means of transmitting the virus.

Recent studies indicate that AIDS is not caused through casual contact. Persons at high risk of HIV infection are homosexuals, bisexuals, heterosexuals with multiple sexual partners, IV drug users, persons who received a blood transfusion from an infected individual, and sexual partners of any of the people in these groups.

The danger of contracting AIDS means that anyone in a high risk group must take precautions to avoid the disease. Persons who have multiple sex partners, or engage in sex with homosexual or bisexual men or with IV drug users should use a condom during sexual intercourse. This significantly reduces the exchange of body fluids. Oral sexual activities should be avoided by high risk groups, also because of the risk of exchanging body fluids.

At particular risk are IV drug users, who share needles to inject illegal drugs. A shared needle contaminated with infectious blood can transmit HIV. IV drug users serve as the major reservoir for transmission of infection to heterosexual adults and their infants, as well as among themselves, according to health officials.

Due to the development of a new test, blood supplies are free of HIV. Thus, worries about blood transfusions have eased considerably. Never has there been danger in giving blood and now there is very little danger in receiving a blood transfusion.

Once the AIDS virus becomes active, the infected person becomes susceptible to a wide variety of illnesses which are not new or unique to AIDS patients. Since the body's immune system no longer functions, people with AIDS are susceptible to many diseases healthy people have an easier time fighting off.

Symptoms of an HIV infection include:

- Severe sustained fatigue.
- Fevers, drenching sweats.
- Weight loss.
- Swollen lymph glands.
- Red or blue skin lesions.
- White spots in the mouth.
- Persistent cough.
- Chronic diarrhea.

Any of these symptoms may indicate HIV infection and a physician should be consulted.

Health officials recommend that persons in high risk groups be tested for HIV. In Indiana, counseling and testing sites have been established in Anderson, Columbus, Evansville, Fort Wayne, Gary, Indianapolis, Richmond, South Bend and Terre Haute. Two sites are also available in Lafayette. Because of the danger of infected persons transmitting the virus to others, it is important that persons who test "antibody positive" be carefully monitored by a physician. In addition, all persons in high risk groups, or who test positive, should practice "safe sex."

clinic in San Francisco General Hospital, is a pioneer in the care of AIDS patients. "In many cases, what we are seeing is adult children returning home to their aging parents who at 60 are not psychologically prepared to care for them. . . ." Dr. Wofsy said we need to respond to this need now so appropriate health care will be available.

While there has been much debate both inside and outside the medical community about testing, the Centers for Disease Control announced recently that it is considering both premarital and hospital admissions screening.

That has caused state health officials to rethink their earlier position on testing of specific groups, said Dr. Myers.

While Dr. Wofsy agreed that testing of specific groups might provide epidemiological information, she indicated she is reluctant to support testing without plans for what to do for those who test positive. "There is no evidence that testing per se will alter somebody's behavior."

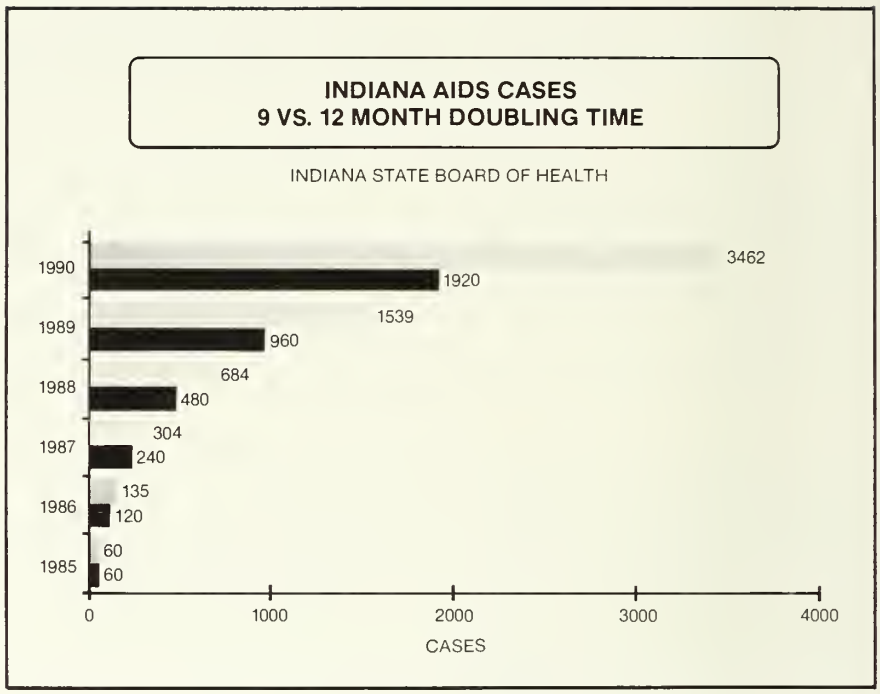
Other issues raised have included the cost of the tests, the number of false-positive tests, confidentiality, and whether hospital admission screening would deter some people from seeking needed hospital care.

Dr. Wofsy said physicians have responded to the disease as people. They have gone through the same phases everyone goes through when met with something new and threatening, including:

- Avoidance.
- Demand that the environment be risk free.
- Realization "AIDS is."
- Interest in self-education.
- Concern for the person with AIDS.

She said that AIDS has been a "pink collar" disease, noting that other conferences she has attended drew more nurses than doctors. Doctors have to remind themselves that the patient is the issue. "As physicians we don't have to agree with it to want to take care of it," she said.

"All staff need to preserve AIDS skills. There is no way health care providers can avoid treating AIDS patients."



CME QUIZ

TO OBTAIN ONE HOUR OF CATEGORY 1 AMA CME CREDIT, answer the following questions by circling the correct answer on the answer sheet below. Complete and clip the application form and mail it to: **Indiana University School of Medicine, CME Division, BR 156, 1226 W. Michigan St., Indianapolis 46223.**

Perinatal Infections

CONTINUED FROM PAGES 323-325

1. Prolonged rupture of the membranes occurs in ____ of all pregnancies.
   a. less than 1%
   b. 1 to 3%
   c. 5 to 10%
   d. 15 to 20%

2. The majority (more than 50%) of infants with sepsis neonatorum belong to this group.
   a. delivered of mothers with PROM
   b. delivered of mothers with clinical amnionitis
   c. delivered of mothers without PROM
   d. none of the above

3. The risk of bacterial sepsis in infants delivered of women with PROM alone is ____.
   a. 0.1%
   b. 1.0%
   c. 10%
   d. 7.2%

4. In early onset neonatal sepsis, the following culture is the most frequently positive and clinically relevant.
   a. CSF
   b. blood
   c. urine
   d. skin

5. What percentage of neonates with septicemia have meningitis?
   a. 25 to 35%
   b. less than 3%
   c. 65 to 75%
   d. none of the above

6. Bacteremia with *Group B Streptococcus* develops in ____ percent of infants colonized with the organisms at birth.
   a. 5-10%
   b. 25-30%
   c. 50-75%
   d. 1-2%

7. Surface cultures from infants born to women with PROM
   a. usually predict septicemia
   b. occasionally are useful as an epidemiologic tool
   c. should be performed in every infant with PROM
   d. both (a) and (c)

8. Which test would be most specific in the first week of life to diagnose congenital infection in an infant with microcephaly and periventricular calcifications?
   a. Viral culture of the urine
   b. IgM antibody titers
   c. IgG antibody titers
   d. Rheumatoid factor

9. The sensitivity of IgM antibody titers in congenital toxoplasmosis is thought to be ____.
   a. 20%
   b. 70%
   c. 90%
   d. 100%

10. Recovery of the infectious agent is most necessary in the diagnosis of congenital ____.
    a. Syphilis
    b. Toxoplasmosis
    c. Rubella
    d. Herpes

MARCH CME QUIZ Answers

Following are the answers to the CME quiz that appeared in the March 1987 issue: "Treatment of Myasthenia Gravis," by Rahman Pourmand, M.D.

1. c	6. b
2. a	7. c
3. e	8. c
4. a	9. e
5. c	10. b

Answer sheet for Quiz: (Perinatal Infections)

1. a b c d	6. a b c d
2. a b c d	7. a b c d
3. a b c d	8. a b c d
4. a b c d	9. a b c d
5. a b c d	10. a b c d

I wish to apply for one hour of category 1 AMA Continuing Medical Education credit through the I.U. School of Medicine. I have read the article and answered the quiz on the answer sheet above. I understand that my answer sheet will be graded confidentially, at no cost to me, and that notification of my successful completion of the quiz (80% of the questions answered correctly) will be directed to me for my application for the Physician's Recognition Award of the American Medical Association. I also understand that if I do not answer 80% of the questions correctly, I will not be advised of my score but the answers will be published in the next issue of INDIANA MEDICINE.

Name (please print or type)

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To be eligible for this month's quiz, send your completed, signed application before May 10, 1987 to the address appearing at the top of this page.



AUXILIARY REPORT

Alfrieda Mackel (Mrs. Frederick)
ISMA Auxiliary President 1986-87

To inspire every Indiana medical auxilian to become informed on medical concerns and issues and to become involved with auxiliary in supporting physicians is an ongoing challenge to the ISMA Auxiliary.

To meet the challenge, the ISMA Auxiliary Board has conducted a series of workshops for Hoosier auxilians this year. The first was in May, early in the year to help county leaders on planning programs. The second, the September Leadership Conference, included two medical concerns, changing methods of medical practice and the liability problem, as well as leadership skills development. A third workshop on the impaired physician and the family is on the agenda of the Auxiliary's annual meeting to be held April 28, 29, 30 in Fort Wayne. These workshops have been effective, and the goal of the Auxiliary is to add a two-day conference to the program next year.

Fourteen Indiana county presidents-elect and four ISMA Auxiliary officers attended AMA Auxiliary workshops, called confluences, in Chicago in September and February. Audio and video cassettes of these leadership training programs and other informational materials published by the AMA Auxiliary have been collected for use in the Indiana workshop program.

The ISMA Auxiliary Board has close communication with county auxilians by visits, telephone calls, letters, and most important of all, by our publication, *The Pulse*.

The effectiveness of our efforts for the year will be measured by total membership increases, by new county auxiliaries, and by programs and projects completed in the counties as reported by county presidents at our Annual House of Delegates meeting this month. All auxilians and their spouses have been invited and urged to attend all or any part of the program.

This Publication is available in Microform.

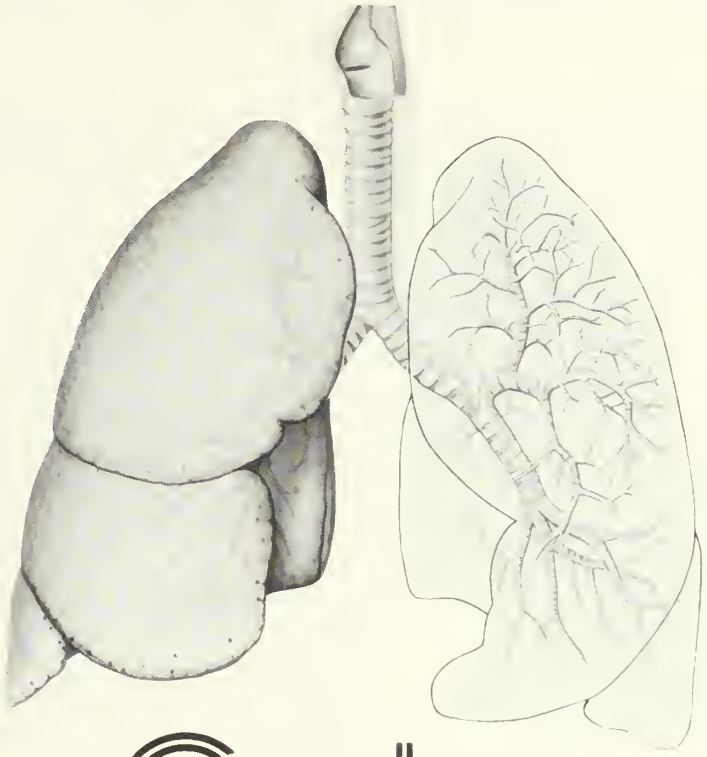


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- In renal impairment, safe dosage of Ceclor may be lower than that usually recommended. Ceclor should be administered with caution in such patients.
- Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.
- Safety and effectiveness have not been determined in pregnancy, lactation, and infants less than one month old. Ceclor penetrates mother's milk. Exercise caution in prescribing for these patients.

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Therapy-related adverse reactions are uncommon. Those reported include:

- Gastrointestinal (mostly diarrhea): 2.5%.
- Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment.
- Hypersensitivity reactions (including morbilliform eruptions, pruritus, urticaria, erythema multiforme, serum-sickness-like reactions): 1.5%; usually subside within a few days after cessation of therapy. These reactions have been reported more frequently in children than in adults and have usually occurred during or following a second course of therapy with Ceclor. No serious sequelae have been reported. Antihistamines and corticosteroids appear to enhance resolution of the syndrome.
- Cases of anaphylaxis have been reported, half of which have occurred in patients with a history of penicillin allergy.
- Other: eosinophilia, 2%; genital pruritus or vaginitis, less than 1%.

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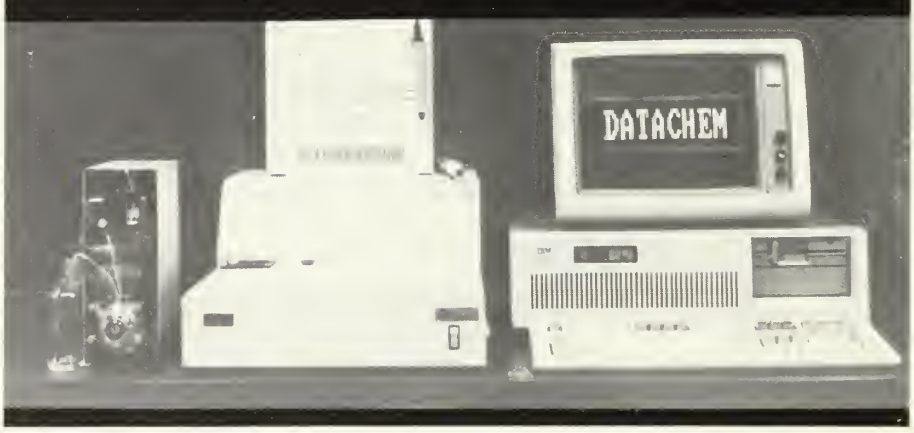
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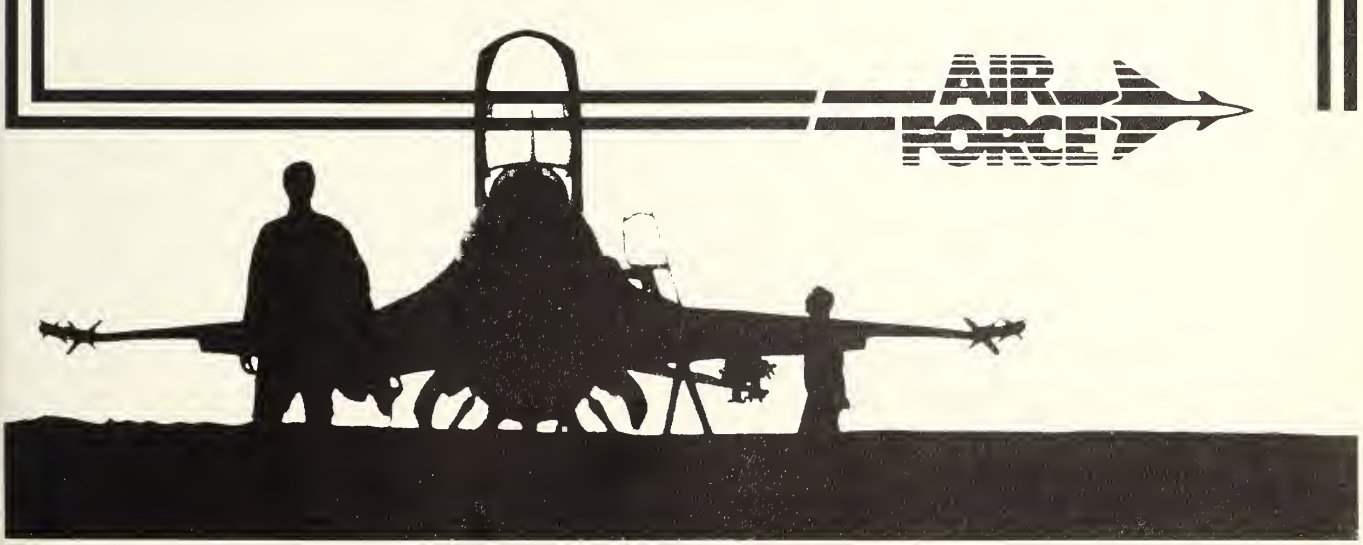
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AIR FORCE



NEWS NOTES

Pathologists Announce Awards Competition for Medical Students

The American Society of Clinical Pathologists (ASCP) will accept entries for the 1988 Sheard-Sanford Awards Competition until Sept. 1, 1987. The program, established in 1928, encourages undergraduate medical research in experimental, clinical and creative morphologic pathology by recognizing outstanding efforts in these areas.

U.S. and Canadian medical students are eligible to enter. To qualify, students must submit a scholarly manuscript to the ASCP based on their research. Each candidate is limited to a single entry. Published manuscripts are acceptable. Each entry must be accompanied by a letter from the pathology department chairman; the letter should describe the candidate's background and confirm that he or she was an undergraduate medical student when the research was conducted. Entry forms are available from the ASCP, Office of the Chief of Staff, 2100 W. Harrison St., Chicago 60612.

Two candidates are honored each year. They receive all-expense paid trips to the ASCP-CAP Spring Meeting, which in 1988 will be in Kansas City, Mo; commemorative medals from Bausch and Lomb, Inc.; and certificates from the ASCP. Royalties from sales of the photelometer developed by Drs. Charles Sheard and Arthur H. Sanford support the program.

NIH Consensus Conferences Planned

Three National Institutes of Health consensus development conferences will be conducted in Bethesda, Md., in June and July.

"The Management of Clinically Localized Prostate Cancer" will be conducted June 15 to 17.

"The Differential Diagnosis of Dementing Diseases" will be considered July 6-8; it is expected that the diagnosis of Alzheimer's disease will be reviewed, as well as the diagnosis of other forms of dementia.

Finally, neurofibromatosis will be the subject for discussion July 13-15.

For the Asking . . .

• "Stress and Illness" is an educational film just released by the American College of Physicians as part of its HEALTHSCOPE series of public health documentaries. The film is available free on loan to companies, hospitals, schools, civic groups and other organizations. (Other films in the series include Chest Pains; Diabetes; Aches, Pains and Arthritis; Shortness of Breath; Stomach Pains; and Eating Disorders.) To arrange for a showing, call toll-free 1-800-222-0025, Monday through Friday, 9 a.m. to 5 p.m.

• "How Much Is Your Practice Really Worth?" is the title of the lead article in the February 1987 issue of "Physician's Advisory." The article details observations of various types of practices in regard to value of good will and other characteristics. Single issues cost $15. The subscription rate is $120 annually (12 issues). Write MCA Publications, P.O. Box 126, Bala Cynwyd, Pa. 19004.

• "Alcohol and Addiction Magazine" announces that a free subscription is being made available for the asking to each of the 400,000 licensed physicians in the United States. The editors urge doctors to "take advantage of this opportunity to acquire new insights and perspectives." The offer expires April 30. Write to the magazine at 23860 Miles Road, Cleveland, Ohio 44128.

• The National Committee for Prevention of Child Abuse has added two new pamphlets to its series. "Emotional Abuse: Words *Can* Hurt" is written by Marla Brassard and Stuart N. Hart; Hart is a faculty member at IUPUI. "Parent-Child Bonding: The Development of Intimacy" is written by Stanley I. Greenspan. For copies, contact the Committee at 332 S. Michigan Ave., Suite 950, Chicago 60604—(312) 663-3520.

Indigent Heart Patients to Receive Free Calan

G.D. Searle & Co. will make $10 million worth of its anti-hypertension and anti-angina drugs, Calan SR and Calan (verapamil HC1), available free of charge to indigent patients.

The announcement was made in mid-February by Sheldon G. Gilgore, Searle chairman, and U.S. Congressman Henry A. Waxman, chairman of the House Commerce Subcommittee on Health and the Environment.

ORAL or WRITTEN

Commentary

For most of us, information is given or sent orally or in writing. Pictures, images of one kind or another, are often formally labeled with the suffix "graph," which comes from the Greek "graphein," and that stem means "to write."

Many people use the word "verbal" instead of "oral" or "spoken" when they are talking about the giving of a report. For example, "I gave him a verbal report," is often heard.

"Verbal" comes from the Latin "verbum," meaning "a word." More specifically, we use verbs to state acts, occurrences, or states of being.

What the person meant who talked about the report is that he gave an oral report or a spoken report; it was something that came out of his mouth.

"Verbal" is used so much in place of "oral" that this usage is recognized by dictionaries. But it always rings a little false to me when I hear it, for after all, the man didn't intend to mean that he had given a *word* report—that's redundant, when you consider the origin of the word. He meant that he gave an oral report—one that came out of his mouth.

I'm not going to try to launch a crusade against "verbal" when "oral" or "spoken" is much better. But I suggest that we think about it.—**Richard J. Noveroske, M.D., Newburgh**

You're the Doctor: What Do You Say?

ISMA's "Your Hoosier Doctor Says" column, published weekly by many Indiana newspapers, needs your ideas and advice.

The columns are short and feature medical information of interest to lay readers. In typewritten form, each column is about one to 1½ pages long, double-spaced.

If you would like to contribute one or more articles, or have information or topics to suggest, please contact Jamie Fillio at ISMA headquarters—(317) 925-7545 or 1-800-382-1721.

I.U. Sets May 20 as Medical Alumni Day

The Indiana University Alumni Association has announced that its annual Medical Alumni Day is scheduled for Wednesday, May 20.

Mr. Charles M. Coffey, director of Alumni Affairs, Indianapolis Campus, has provided the following tentative schedule:

10 a.m.—Annual business meeting of the Medical Alumni Association;

11 a.m.—Development preview program marking the construction of the Medical Research and Library Building.

Noon—Medical Alumni Day luncheon.

The luncheon will be conducted under the red-and-white tent on the east lawn of the Union Building at the I.U. Medical Center. Advance tickets are $19.50; at the door, they will be $21. Advance tickets may be purchased through the Alumni Office, 620 Union Drive, IUPUI, Indianapolis 46202—or call (317) 274-8828.

Help for Refugees

Since the Soviet invasion of Afghanistan in December 1979, about one million Afghans have died and four to five million are now refugees in Pakistan and Iran.

Victims of the conflict can be brought to the U.S. if pro bono care can be obtained. Organizations are available to allow medical volunteers to provide care for refugees in camps in Pakistan, and to participate in training paramedical people who provide medical services in Afghanistan.

Members of the Indiana medical community interested in receiving information on this program should contact Richard S. Idler, M.D., Indiana Center for Surgery and Rehabilitation of the Hand, P.O. Box 80434, Indianapolis 46280—(317) 875-9105.

Researchers Locate Gene for Alzheimer's Disease

The gene for familial Alzheimer's disease (FAD) is located on the human chromosome 21, says an international group of researchers whose breakthrough findings were published in the Feb. 20 issue of the journal *Science*.

Two DNA markers were found by a research team headed by Drs. Peter St. George-Hyslop and James S. Gusella at Massachusetts General Hospital.

Mapped out by Dr. P. Michael Conneally and Dr. Jonathan Haines at Indiana University School of Medicine, the markers showed that the gene resides in a portion of chromosome 21 that also carries a protein gene recently found responsible for the accumulation of deposits of a fibril protein, called amyloid, in the brain. (This finding also was published in the same issue of *Science*.)

Physician Recognition Awards

The following ISMA physicians are recent recipients of the AMA's Physician Recognition Award. This award is official documentation of Continuing Medical Education hours earned, and is acceptable proof in most states requiring CME in re-registration that the mandatory hours of CME have been accomplished.

Acton, Charles M., Terre Haute
Arab, Mohammad K., LaPorte
Antalik, Thomas J., Muncie
Bermudez-Webb, Nini M., Indianapolis
Biegel, Angenieta A., Indianapolis
Bolinger, Garry L., Indianapolis
Brown, Thomas C., Vincennes
Byrne, Frank D., Fort Wayne
Carey, John A., Gary
Elleman, John H., Kokomo
Erenoglu, Ender, Highland
Feldman, Howard E., Munster
Hayhurst, Thomas E., Fort Wayne
Kane, Jack L., Indianapolis
Kojouharov, Anton N., Fort Wayne
Kroh, Casey, Fort Wayne
Miller, David A., Indianapolis
Nasr, Amin T., Muncie
Norins, Arthur L., Indianapolis
Peters, Elmer E., Brookville
Pond, William W., Fort Wayne
Prasertwanitch, Yupadi, Granger
Pruitt, Jacob E., Merrillville
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Salberg, Larry M., Merrillville
Schafer, Scott W., Logansport
Schalliol, James P., Rochester
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Steele, Robert J., Kokomo
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Wass, Justin L., Indianapolis
Watson, Leo G., Kokomo
Woodruff, Richard N., Richmond
Young, Eusebio C., Carmel
Young, Steven R., Carmel

NEWS NOTES

Here and There . . .

Drs. Richard S. Idler and R. Daniel Zieg of Indianapolis have been inducted as fellows of the American Academy of Orthopaedic Surgeons.

Dr. Ronald G. Blankenbaker of Indianapolis is the new president of Hoosiers for Safety Belts; Dr. Thomas C. Madden of Bloomington is vice-president of the coalition.

Dr. Baron L. Kidd of Indianapolis has received the Edward M. Micon Teaching Award in recognition of his service with the St. Francis Hospital Family Practice Residency Program.

Dr. William E. Weber has been elected chief of the medical staff, Bloomington Hospital; Dr. Walter L. Owens is chief of staff-elect.

Dr. Don C. Fields, a Lafayette general surgeon who had practiced since 1958 at the Arnett Clinic, has retired from practice.

Dr. Primo A. Andres of Terre Haute was campaign chairman of the American Heart Association's 1987 fund-raising drive in Vigo County.

Dr. David H. Jones of Charlestown has been elected to the board of directors, Indiana Southern Bank.

Dr. Robert B. Kolbe is the new president of the medical staff, Community Hospital of Bremen.

Drs. Fred M. Blix and Timothy J. Kelly of Indianapolis and Dr. Bryce B. Rohrer of Harvey, Ill., have been certified by the American Medical Society on Alcoholism and Other Drug Dependencies as experts in treating chemical dependency.

Dr. Garland E. Byron is the new president of the medical staff, Home Hospital, Lafayette; Dr. Edward L. Langston is president-elect, and Dr. Barbara J. Bourland is secretary-treasurer.

Dr. C.R. Slick, a Winchester family physician, has retired from practice.

Dr. Gregory A. Hoffman of Fort Wayne is a new fellow of the American Academy of Orthopaedic Surgeons.

Dr. Frederick M. Kelvin, an Indianapolis radiologist, is first author of *Clinical Imaging of the Colon and Rectum*, a book just published by Raven Press, New York.

Dr. Harry R. Stimson is the new president of the medical staff, St. Joseph's Medical Center, South Bend; Dr. Daniel W. Kletzing is vice-president, and Dr. Jan C. Green is secretary-treasurer.

Dr. Frederick B. Stehman of Indianapolis has been named chief of obstetrics and gynecology, Wishard Memorial Hospital.

Dr. George W. Macy, a Columbus general surgeon, has retired from practice.

Dr. Jerry L. House of Indianapolis recently participated in an ENT Board Review Course in Chicago; he presented two lectures, "Temporal Bone Surgery" and "Audiologic Testing;" he also gave a lecture on "Temporal Bone Tumors" at an ENT Board Course last month.

Dr. Howard J. Henry, a Knox family physician 40 years, has retired from practice.

Dr. David S. Batt, an Indianapolis rheumatologist, discussed arthritis during a January public forum at the Greensburg Nursing Home.

Dr. William J. Lewis, a Fort Wayne neonatologist, was guest speaker at the January Caylor-Nickel Medical Center's Nursing Grand Rounds in Bluffton.

Dr. Phil O. Burgan is the new chief of the medical staff at St. Joseph Hospital, Kokomo; Dr. John Ayers is chief of staff-elect, and Dr. Willis W. Peelle is secretary.

Dr. John J. Mulcahy, an Indianapolis urologist, directed a panel discussion during the February meeting in Indianapolis of the Indiana Impotence Support Group.

Correction

INDIANA MEDICINE incorrectly reported in its February 1987 issue that Dr. Kenneth R. Woolling of Indianapolis has retired.

Dr. Woolling has closed his office for the private practice of cardiovascular disease and internal medicine, which he has maintained for 34 years, but he will continue to serve as a consultant in vascular medicine.

Dr. A.R. Rao of Kokomo was guest speaker at the February meeting of the Kokomo Area Ostomy Chapter.

Dr. Gerry M. Hippensteel of Vincennes discussed chemotherapy at the January meeting in Vincennes of "Families Facing Cancer."

Dr. James T. Walsh of Terre Haute was a guest speaker at the February meeting in Terre Haute of the Alzheimer's Family Support Group.

Dr. Louie O. Dayson, a Vincennes cardiologist, was guest speaker at the February meeting in Vincennes of the Knights of Columbus Ladies Auxiliary.

Dr. Stephen W. Perkins of Indianapolis lectured on "Liposuction of the Neck" during the January Midwestern regional meeting in Cleveland of the American Academy of Facial Plastic and Reconstructive Surgery; Dr. Ronald C. Hamaker of Indianapolis lectured on "Cosmetic Surgery in Head and Neck Cancer Patients" and was a panel member for discussions on "Tissue Expansion."

Dr. Randolph W. Lievertz of Indianapolis was on the lecture circuit in January and February, presenting talks on menopause, osteoporosis, pneumonia, and treatment of skin infections in Fort Wayne, Indianapolis, Kalamazoo, Lansing, Detroit, Milwaukee, St. Paul, Minn., and Wausau, Wisc.

Facsimile Machine Allows Scientific Link with China

What is believed to be the first permanent facsimile hook-up between scientific health institutions in the People's Republic of China and the United States was made possible recently as the result of a grant from the American Institute for Cancer Research.

The Chinese Academy of Preventive Medicine in Beijing was presented a Sharp brand fascimile machine that will allow research data to be transmitted directly between the Academy, Cornell University (N.Y.) and Oxford University (England). The machine will be used in support of a joint research effort being conducted by Chinese, American and English scientists.

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OBITUARIES

Robert Hayter, M.D.

Dr. Hayter, 75, a former Lyons surgeon who retired last year, died Jan. 9 in Oregon.

He earned the M.D. degree in 1940 from the University of Oregon. He was a Navy veteran of World War II.

Dr. Hayter lived and practiced in Waldport, Ore., after leaving Indiana several years ago.

Harold W. Williams, M.D.

Dr. Williams, 61, an Indianapolis physician, died Dec. 26 at Community Hospital, Indianapolis.

He was a 1958 graduate of Indiana University School of Medicine and was a Navy veteran of World War II.

Dr. Williams had been associated with Castleton Family Physicians and was a Community Hospital board member. He was a fellow of the American Academy of Family Physicians and was certified by the American Board of Family Practice.

Wenceslao Magbag, M.D.

Dr. Magbag, 72, a retired Holland urologist, died Jan. 2 at Welborn Memorial Hospital, Evansville.

He received his M.D. degree in 1941 from the University of Santo Tomas, the Philippines.

Dr. Magbag was a former secretary of the Dubois County Medical Society. He had been a staff member at St. Joseph's Hospital, Huntingburg.

James M. McFadden, M.D.

Dr. McFadden, 75, a retired Lafayette pathologist, died Jan. 17 at his home.

He was a 1936 graduate of Indiana University School of Medicine. He was an Army veteran of World War II and served in the Indiana National Guard 30 years.

Dr. McFadden founded the Professional Associates Laboratory in Lafayette, which he operated from 1956 until he retired in 1984. He was a fellow of the American Society of Clinical Pathologists and the American College of Pathologists. He was a life fellow of the American College of Physicians, and he became a member of the ISMA Fifty Year Club last year.

Dorothy Ruth Darling, M.D.

Dr. Darling, 72, a retired Merrillville anesthesiologist, died Jan. 23 at Methodist Hospital Southlake Campus.

She was a 1941 graduate of Indiana University School of Medicine.

Dr. Darling had practiced at Methodist Hospital in Merrillville and in Gary for 35 years. She was the senior staff anesthesiologist at Gary Methodist 23 years. She was a member of the American Society of Anesthesiologists and a former vice-president of the American Medical Women's Association. Last year, she won the AMWA's Camille Mermod Award.

Richard R. Hughes, M.D.

Dr. Hughes, 68, a retired Lafayette general surgeon, died Feb. 17 at St. Elizabeth Hospital Medical Center.

He was a 1943 graduate of Indiana University School of Medicine and was an Army veteran of World War II.

Dr. Hughes, a diplomate of the American Board of Surgery, was a fellow of the American College of Surgeons and the American College of Emergency Physicians. Before retiring, he had been associated with St. Elizabeth Hospital Medical Center and Home Hospital in Lafayette.

Paul L. Stier, M.D.

Dr. Stier, 79, a retired Fort Wayne internist, died Jan. 27 at Miller's Merry Manor, Fort Wayne.

He was a 1933 graduate of Indiana University School of Medicine and a Navy veteran of World War II.

Dr. Stier, a life-long Fort Wayne resident, was a past president of the Fort Wayne Medical Society and was a member of the ISMA Fifty Year Club. He was a co-founder of the American Heart Association's Northeast Indiana Chapter and was active in its operation for several years.

Thomas E. Reed, M.D.

Dr. Reed, 54, a retired Indianapolis family physician, died Jan. 28 at his home.

He was a 1963 magna cum laude graduate of Indiana University School of Medicine and was an Army veteran of the Korean War.

Dr. Reed specialized in family medicine at Community Hospital, Indianapolis, for several years and had been medical director, Indiana Blue Cross and Blue Shield.

Memorials: Indiana Medical Foundation

The Indiana Medical Foundation, Inc. was formed by the Indiana State Medical Association "for religious, charitable, scientific, literary or educational purposes." It provides financial assistance to support the educational mission of INDIANA MEDICINE.

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COMMERCIAL ANNOUNCEMENTS

PEDIATRICS: Southeastern Wisconsin. Large multi-specialty group located near Milwaukee is seeking a fourth BE/BC pediatrician. Competitive salary, excellent fringe benefits. Address inquiries and CV to Administrator, P.O. Box 427, Menomonee Falls, Wisconsin 53051.

GENERAL INTERNIST/FULL-TIME position with a growing multispecialty group involved in both prepaid and fee-for-service practice. Group ventures include 24-hour priority care center and a development of satellite offices. Internal med practice approximately 50% primary care. An excellent opportunity to grow in an economically dynamic northeastern Indiana community. Salary and full benefit package. Contact M.G. Hawkins at 3301 Lake Ave., Fort Wayne, Indiana 46805—(219) 422-8487.

CHILD/ADOLESCENT PSYCHIATRIST needed, Board-eligible, preferred certified, to work closely with a multidisciplinary team in an accredited 40-bed child and adolescent psychiatric hospital, an agency of the Michigan Department of Mental Health. We are located in beautiful Traverse City, Michigan. A water and winter wonderland. Traverse City is the cultural and medical center for northern Michigan. Skiing, fishing, hunting and sailing are at your doorstep. We have an excellent school system and a pollution free, low crime environment. Salary depending upon qualifications to $86,000, with remarkable fringe benefits. Send curriculum vitae and three letters of reference to Arnell Engstrom Children's Center, Box C, Traverse City, Michigan 49684, or call Robert E. Davidson, M.D., or Paul Surratt, Ph.D., at (616) 922-5400. An Equal Employment Opportunity Employer.

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PHYSICAL THERAPY—An individual with 17 years experience in physical therapy and rehabilitation would like to share the office with a group of orthopedists or family practitioners with good referral potential. The location should be Indianapolis or within 50-mile radius. Please call (317) 888-3856 after 5 p.m.

JOB OPPORTUNITIES—Needed immediately: 2 Family Practitioners (will accept in practice; prefer resident). Location: Central Indiana. Positions are as follows: **Hospital**: Will provide necessary staff, equipment, office space, maintenance, billing and overhead. Numerous benefits in travel, education, insurance for self and dependents, 4 weeks paid vacation plus meeting time. Doctor will be free to practice independently and must share equally in ER. Six-month evaluation and negotiation. **Private Practice**: Broad interest activity; gross $225,000 last year. Salary 1 year, then buy into practice. Call sharing. Salary: $60,000 plus productivity incentive to $75,000+. Contact: Sally J. Raikes, Senior Recruiter, R. Stoll & Associates, Inc., 420 S. Fourth St., Elkhart, Indiana 46516—(219) 522-2396.

FOR SALE—Heading medical equipment. Bell-Tone audiometer, examining tables, baby scales, secretary chairs, waiting room furniture, step-on wastecans, blood pressure wall units, table paper, glass containers. (317) 846-1896.

OB/GYN, ORTHOPEDIC SURGEON: Board certified or eligible to join 15-member group in progressive northwestern Wisconsin community. Modern, well equipped hospital located adjacent to our facility. Close to Minneapolis, Eau Claire and Duluth, the Rice Lake area offers excellent educational, religious and community activities in addition to exceptional sports, hunting, fishing and recreational opportunities. For more detailed information regarding our group, please contact Mark T. Mymo, M.D., Indianhead Medical Group, 1020 Lakeshore Drive, Rice Lake, WI 54868—(715) 234-9031.

FOR LEASE/RENT: 1100 sq. ft. in doctors' building, equipped. Located in Indiana west of Cincinnati; Cincinnati telephone; 2,000 families in growing rural urban community. Call after 5 p.m. EST 812-637-3364, or write Box 248, Rt. 2, Lawrenceburg, IN 47025.

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OPHTHALMOLOGY: Southeastern Wisconsin. Large multi-specialty clinic located near Milwaukee is seeking a second BE/BC ophthalmologist. Non-surgical orientation preferred. Excellent salary and fringe benefits. Interested parties please send inquiries and CV to Joe Schnoll, Mgr., Physician Recruitment, P.O. Box 427, Menomonee Falls, WI 53051.

INDIANA, North of Indianapolis—Immediate full-time and part-time positions in newly renovated emergency department at 135-bed facility. Hourly salary, flexible scheduling, malpractice insurance provided. For more information, contact: Emergency Consultants, Inc., 2240 South Airport Road, Room 19, Traverse City, MI 49684; 1-800-253-1795 or in Michigan 1-800-632-3496.

EMERGENCY MEDICINE POSITION AVAILABLE: Excellent opportunity for experienced emergency physician to join career emergency group practicing in northwestern Indiana, near Chicago. If you have over 4,000 hours experience, please contact Laurie Perkins at (312) 327-0777.

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All orders must be in writing and will automatically be set in regular classified type. *Box numbers are not available.*

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SPRING VACATION: MARCO ISLAND, FL: March 27-April 3 and April 4-11, 1987; beachfront condo for rent, 2 br, 2 ba, sleeps six, low-rise, vaulted ceiling, washer/dryer, walk right onto beautiful beach. Fantastic sunsets, pool, tennis, Jacuzzi, water sports on site, golf nearby. Call (317) 848-0001 after 6:00.

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INTERNAL MEDICINE—Near Indianapolis. Eight-physician group seeks third internist. 90-bed hospital built in 1981. Competitive salary/benefit package. Phil Kelbe, Fox Hill Associates, 250 Regency Ct., Waukesha, WI 53186—(414) 785-6500.

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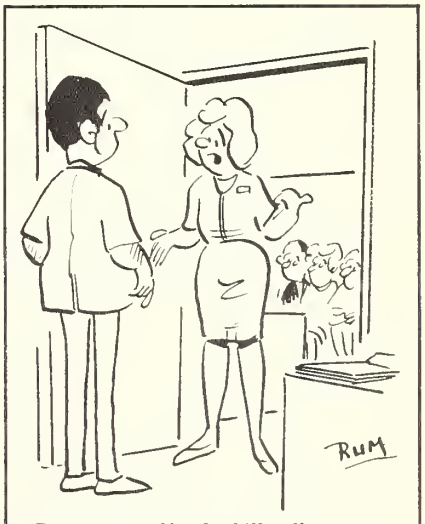
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For more information or to order copies, write to the ISMA Membership Department, Attn: Rosanna Iler, 3935 N. Meridian St., Indianapolis, Ind. 46208.

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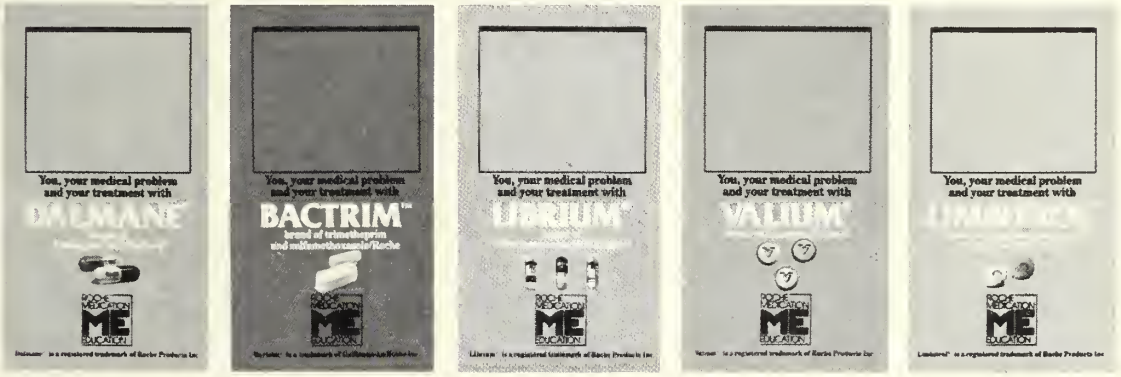
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